Investigating prevalence and healthcare use of children with complex healthcare needs using data linkage

A study using multi-ethnic data from an ongoing prospective cohort: the Born in Bradford project

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Abstract

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Keywords: Primary care, healthcare use, children, complex healthcare needs, congenital anomalies, data linkage, public health, National Health Service

Background:

The impact children with complex healthcare needs have on the healthcare system is significant and requires a multidisciplinary response. Congenital anomaly (CA) is a group of conditions requiring complex and variable input from primary and secondary healthcare. This thesis explores the literature on health system preparedness for children with complex healthcare needs and quantitatively describes healthcare use for a population of children with CA, an exemplar for children with complex healthcare needs.

Methods:

Routine health data from primary care was explored to identify children with CA and linked to secondary care data, outpatient records, and questionnaire data from a multi-ethnic prospective birth cohort over a five-year period. Rates of CA were calculated and healthcare use for children with and without CA was analysed.

Results:

Out of a birth cohort of 13,857 children, 860 had a CA. Using primary care data for children aged 0 to 5 years, the number of children with CA was found to be 620.6 per 10,000 live births, above the national rate of 226.5 per 10,000 live births. Healthcare use was higher for children with CA than those without CA. Demand for use of hospital services for children with CA was higher (Incident rate ratio (IRR) 4.38, 95% confidence interval (CI) 3.90 to

4.92) than demand for primary care services (IRR, 1.27, 95% CI 1.20 to 1.35).

Conclusion:

These results suggest that using primary care data as a source of CA case ascertainment reveals more children with CA than previously thought. These results have significant implications for commissioning healthcare services for children with complex healthcare needs.

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Publications arising from or associated with this thesis

A shortened version of Chapter 2 was published in 2015:

Bishop, C., Small, N., Parslow, R. and Bowles, D., 2015. Improving service coordination for children with complex needs. *British Journal of Healthcare Management*, *21*(10), pp.469-475.

The analyses of congenital anomaly case ascertainment using primary care data has been published in BMJ Paediatrics with the following authors and title:

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1 Introduction

1.1 Background

This thesis presents the findings of an investigation into the prevalence rates of children with complex healthcare needs in the multi-ethnic city of Bradford, and the impact that responding to their needs has on healthcare services. Central to doing both of these things is the use of data linkage. Children with complex healthcare needs are defined as children who are likely to have a combination of physical and social needs, requiring input from a range of different services including those provided by health and social care, which are likely to persist over an extended period of time (Department of Health, Social Services & Public Safety; DHSSPS 2007).

It is documented that children and young people with complex healthcare needs have not been particularly well served by the National Health Service (NHS) and Social Services in the past (Department of Health; DH 2014). Identified shortcomings include responding to children's needs with disjointed services, sometimes due to the novelty of the disease, sometimes due to overly complicated patient pathways, and exacerbated by the divide between primary care, community and hospital services (NHS England 2014). Consequently, the ability to manage long-term conditions, sometimes conditions without a precise diagnosis, becomes complex for families, carers and the healthcare services. This creates a situation where there may be a great impact on families and those that care for children with complex healthcare needs because of a lack of appropriate and integrated care. One way of measuring the extent of children's multidisciplinary healthcare needs (in order to propose solutions) is to use data linkage, a method that combines several sources of routine health data together, to obtain a multi-service perspective of healthcare use for individual people.

As the number of children with complex healthcare needs rises, so too does the cost to the healthcare service. Overall costs associated with complex cases are difficult to define because of variations in medical practice, shortages in healthcare resources (which may mean needs are not met) and the multidisciplinary needs of children with complex conditions necessitating services from various sources (Freeman and Hughes 2010). Healthcare providers need to work together and communicate effectively to meet these children's needs (DH 2013b). In order to understand, influence and improve services for children with complex healthcare needs, accurate measurements of the healthcare services supporting them are required. These measurements can also be used to enable those responsible for commissioning and delivering healthcare to make effective decisions about the provision of healthcare services, ensuring children receive the best possible care (HQIP 2015).

While a greater understanding of the care needs for children with complex needs will provide the evidence to help improve standards of care, applying improved standards of care, and ensuring they are maintained, requires the collection of high-quality data (Horridge et al. 2015). However, there are many different childhood conditions that might be considered complex, making data collection difficult and unfocused. While it might be expected that children with complex healthcare needs place a larger demand on the healthcare service than children without complex healthcare needs, in order to measure the extent of this impact and understand what elements of their care contribute to it, a specific and representative study population is required.

Rather than trying to capture every child with complex healthcare needs, this thesis focuses its study on children with congenital anomalies (CA). The wide-ranging disability profile of children with CA means this group of disorders serves as an exemplar of children with complex healthcare needs, as they typify the kind of complexity experienced from a range of disabling conditions. CA is also one of the leading causes of death and disability in the UK (CA) (Office for National Statistics; ONS 2015a). For children who survive, CA has a debilitating impact on their health, with a wide-ranging profile of disabilities affecting many

bodily systems (Horridge et al. 2015). CA is also a priority for global research. A key intervention of the 63rd World Health Assembly (WHO 2010a) was to promote the health of children with CA, due to concerns regarding the high levels of neonatal deaths occurring from CA worldwide. The key recommendations included strengthening surveillance systems and improving diagnosis and prevention. Around 93% of children with CA are surviving into adulthood, and with relatively little known about their long-term needs or the consequences of CA (Sokal et al. 2013), this is an area that warrants further investigation.

1.2 Definitions

Congenital anomaly

The WHO (2016) defines a CA as a congenital disorder, also known as a birth defect, which can be structural or functional and occurs during the intrauterine period. Dependent on type, they can be identified prenatally, at birth or in later life. When the term prevalence is mentioned in this thesis, it should be interpreted as the 'birth prevalence' of CA, as prevalence on its own refers to the proportion of pregnancies, not the proportion of live births in a population (Cornel 1999). It is important to report the birth prevalence of CA as so many of those affected die very young, which skews the population prevalence and usually results in the population prevalence of birth defects being much lower than birth prevalence (Christianson et al. 2006). CA is an abnormality of structure, function or metabolism present at birth, which may result in a mental, physical disability or fatality (Misra et al. 2005). CA is not just a cause for concern in Bradford or the UK, as it has significant health implications worldwide. It is estimated that 7.9 million children globally are born with a serious CA, and, despite it being possible for some of these to be managed and treated, an estimated 3.2 million children remain disabled for life (Lobo and Zhaurova 2008). The World Health Organisation (WHO; 2016) considers CA as

a cause of long-term disability, with a significant impact on individuals, families and healthcare systems.

Complex healthcare systems

The WHO refers to complex healthcare systems as composed of networks of interconnected components that influence each other, often in a nonlinear fashion (Amaral and Ottino 2004).

Healthcare use

The McGraw-Hill Concise Dictionary of Modern Medicine (Segen 2006) defines healthcare use as:

> '*The use or amount of usage of healthcare services per unit of the population, or the pattern of use of a service or type of service in a specified time, usually specified in rate per unit of population-at-risk for a given period' (Segen 2006: 112)*

Children with complex healthcare needs

Children with complex healthcare needs are likely to have a combination of complex physical needs, requiring a range of ongoing and multi-agency services, beyond the needs of children generally (Department of Health, Social Services & Public Safety; DHSSPS 2007). The Scottish Complex Healthcare Needs Group uses the following definition for children with complex healthcare needs:

> '*The child has severe or profound disabilities in at least three of the following categories or the child has severe or profound disabilities in at least two of the following disability categories plus need of at least two types of resources. In either case the impairments and needs of these children are sustained lasting for more than 6 months and ongoing' (DHSSPS 2007: 25)*

Disability Categories

- Motor Impairment
- Hearing impairment
- Visual impairment
- Cognitive impairment
- Speech and language impairment
- Behaviour problems
- Feeding problems
- Additional Chronic health needs

The English version of this definition was reported most recently by the Council for Disabled Children (2017), who state that children and young people whose disabilities have a significant and enduring impact on their life are likely to need specialist support from education, health and/or social care regularly. These children are likely to be known to child development teams (healthcare), disabled children's teams (social services) and have had a learning difficulty assessment. This definition encompasses both physical and cognitive impairments as well as a need for services.

Routine health data

Large amounts of data is routinely generated by healthcare organisations, providing analytical opportunities for healthcare research. Routine health data includes data that is produced through clinical encounters, in both primary and secondary care, and it sometimes also includes data from disease registers and public health surveillance among others. Because routine health data is not originally collected for research, the exact data availability and sources differ, meaning linkage between several sources is sometimes needed to both improve the quality and completeness of a dataset and to answer particular research questions. Making the most of routine health data is recognised by the NHS Five Year Forward Review for a 'paperless' NHS by 2020 (NHS England 2014). These paperless plans are outlined further in the National Information

Governance Board document ‘Personalised health and care 2020: Using data and technology to transform outcomes for patients and citizens: a framework for action’ (HM Government 2014).

Data linkage

Data or record linkage has been defined as ‘a process of pairing records from two files and trying to select the pairs that belong to the same entity’ (Bohensky et al 2010: 1). Data linkage may be conducted between two distinct data sources or within a single dataset to identify multiple entries (e.g. re-admissions) for one person (Bohensky et al. 2010). The increased use of existing data resources, made available through improved access arrangements and data linkage, is currently one of the most cost-effective ways of supporting research in public health and epidemiology (Wellcome Trust 2015).

1.3 Overview of policy shaping children’s services

While there is an abundance of policy and legislation that aims to shape healthcare practice in relation to children, the recommendations that arise from this are far from linear. This adds complications when trying to pinpoint a particular aspect of practice that needs improving in children’s care. Poor agreement on how to define the service requirements of children with complex healthcare needs, exactly what data to collect, and a variation in the terminology and data collection systems used, make commissioning services for these children difficult (Council for Disabled Children 2017). Variations in outcomes and quality of healthcare for children and young people have been noted consistently as a key area for improvement by the Department of Health (DH 2013a, DH 2013b, DH 2013c). Complex healthcare needs as a criterion for classifying a subgroup of children is gradually being recognised by health authorities, yet there is still much work to be done around implementation and evaluation of services.

One government initiative proposed that children with Special Educational and Complex healthcare needs (SEND) (DH 2014) require individual needs assessments, with greater focus on joint working between health, education and social care. The latest Children and Families Act (The Stationery Office 2014) introduced Education Healthcare Plans from the 1st September 2014, which initiated statutory and coordinated assessments across education, health and care. These coordinated assessments must reflect the views of families and children and they advocate person-centred care coordination. Across the UK each Clinical Commissioning Group (CCG) now has statutory duties to liaise with relevant local authorities in a coordinated assessment of each child's need (Department for Education 2014a). It is noted, however, that SEND has not been as successful in shaping health services as it has in education and social care. This is partly attributable to the lack of explicit guidance from the DH on how to engage with the SEND pathfinder. It is also due to a common dilemma in health when dealing with re-organisation of the health service, in that disruptions occur when senior health professionals struggle to balance the demands of service improvement and their core health work (Department for Education 2014a).

Some solutions to improving care coordination of health services include the Chief Medical Officer's (2013b) proposal for named General Practitioners (GPs) for each child. The Royal College of Paediatrics and Child Health (2014) also recognises the need for designated named professionals, who have a responsibility for managing the healthcare of children whose needs are complex. The Child Health Promotion Program (DH 2004) aims to facilitate early recognition of disability and complex healthcare needs in children that are likely to require specialist services, earmarking them for regular developmental reviews. Developmental reviews are a central component of the Chief Medical Officer's (DH 2013b) proposal for a child passport, a document containing updated information on each child's functional and medical capacity, thus reducing the need for repeated assessments each time a child requires services.

Improving Children and Young Peoples Heath Outcomes (DH 2013c) is a further key policy driver. It investigates unexplained variation in aspects of children's healthcare and makes the case for integrated care. Longitudinal data depicting children's care needs in five-year age bands is investigated, starting from their first NHS presentation, to time of diagnosis or start of treatment (DH 2013c). At present, these investigations into variations in care have created incentives for driving service improvement, but have not reached an implementation and evaluation phase to determine if variations in care are reducing for children. The DH (2014a) advises that in order to accurately ascertain the local needs of those using healthcare services, access, referrals to outpatients, and qualitative aspects (such as speaking to those with direct experience of service delivery) need to be captured.

In order to make meaningful changes to a healthcare system, there needs to be some proof that the planned changes accurately meet demand. Previous research seeking to improve the quality of care for children with disabilities and complex healthcare needs has noted the lack of high-quality data on existing best practice, as the UK currently has no national data collection system to produce comprehensive population-based evidence of this kind (Horridge et al. 2015). The Chief Medical Officer (2013b) has also noted the lack of robust quantitative analysis on children's long-term health outcomes when this analysis is compared to similar studies on adults. Information trends are also lacking, with estimates on prevalence completely dependent on the diagnostic criteria available from primary care (DH 2013b). Neglecting the translation of data outlining healthcare use into practical solutions to improve the planning support for children with complex healthcare needs is a missed opportunity (Council for Disabled Children 2017). The Children and Young Peoples Outcomes Forum (DH 2012) also argues that the lack of data for children with disabilities results from the complexity of their needs, the many contact points they have with the health services and their relationships with different healthcare professionals. All these things make them difficult to track.

1.4 Rationale

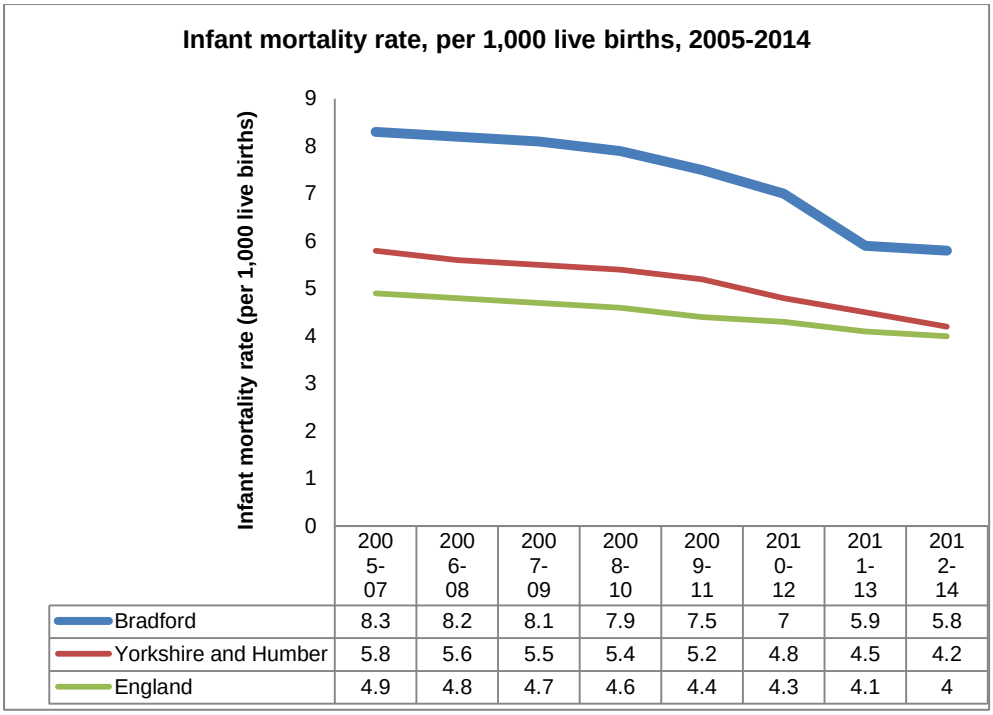
1.4.1 The Born in Bradford Project

As mentioned in Section 1.1, rather than attempting to explore the demand on the healthcare system for all children with complex healthcare needs, a representative study population was required. CA were chosen as an exemplar for children with complex healthcare needs, not only because of wide-ranging disability profiles for children with CA, but also because CA has a particularly high prevalence in the city of Bradford (Sheridan et al. 2013). Bradford is a city in the North of the United Kingdom (UK) with a comparatively high number of children with long-term, complex and sometimes unknown disabilities when compared to the rest of the UK (Child Death Overview Panel; CDOP 2016). Born in Bradford (BiB) is an observational prospective birth cohort study that monitors the health of mothers, their partners and 13,857 children (Wright et al. 2013). This research uses BiB data to report the prevalence of children with complex healthcare needs in Bradford.

Cohort studies are one of the most powerful epidemiological tools as they use large groups of individuals to investigate the natural causes of diseases over time (Law and Pascoe 2013). The aim of the BiB project is to explore the causes of childhood illness as they manifest in different cultural backgrounds and develop interventions to support the health and development of these children. Detailed information is recorded about the cohort participants' demographics, deprivation, clinical outcomes and risk factors. To be eligible for the BiB study, women had to attend the antenatal service in Bradford between March 2007 and December 2011, and be booked to give birth in Bradford (Wright et al. 2013). Over the last decade, there has been a 6% increase in people of Pakistani origin living in Bradford, and, at a total of 20.3%, the Bradford district has the largest percentage of people of Pakistani origin in England. These trends in migration and population growth link the Bradford district with Pakistan by both country of origin, language and faith (Bradford

Metropolitan District Council 2013). The children in the BiB cohort are 50.1% South Asian origin, and 49.9% Non-South Asian (Wright et al. 2013).

There are some other unique characteristics about Bradford, aside from the high prevalence of CA, that make it an ideal population for studying children with complex healthcare needs. Firstly, Bradford's population is large and growing rapidly, at a rate of 11.1% compared to 7.1% nationally. Bradford is also the English city with the youngest population outside London. Over the last decade, the population of 0 to 4 year olds has increased by 20% and almost 25% of the Bradford population is aged under 16 (Bradford Safeguarding Children Board 2016). These demographics and level of growth have and will continue to have significant impact on the health service providing care for young children (Bradford Metropolitan Council 2013). Bradford has also had a consistently high infant mortality rate compared to the national average (Small 2012, Middlemiss et al. 2009). Infant mortality, which is defined as the number of deaths in the first year of life per 1,000 live births, reached a peak in Bradford in 2003, at 9.4 deaths/1,000 live births, when the national average was 5.5 deaths/1,000 live births (Wright et al. 2013). The most recent statistics on infant mortality demonstrate a reduction in rates across the UK generally but Bradford maintains a consistently higher rate at 5.8 deaths per/1,000 live births, compared to 4.0 deaths per/1,000 nationally (CDOP 2016) (Figure 1).



	2005-07	2006-08	2007-09	2008-10	2009-11	2010-12	2011-13	2012-14
Bradford	8.3	8.2	8.1	7.9	7.5	7	5.9	5.8
Yorkshire and Humber	5.8	5.6	5.5	5.4	5.2	4.8	4.5	4.2
England	4.9	4.8	4.7	4.6	4.4	4.3	4.1	4

Figure 1: Rates of infant mortality per/1,000 live births. Bradford/England comparisons (CDOP 2016)

The CDOP (2016) was set up to investigate the consistently high levels of infant mortality in Bradford compared to the rest of the UK. The CDOP (2016) uncovered the most common cause of infant mortality in Bradford as being CA (42%), followed by perinatal and neonatal events (31%) (CDOP 2016). UK wide, the most common cause of death for South Asian babies was also CA at 51.2% of all deaths (ONS 2015a). Immaturity-related conditions were the second most common cause of death overall at 41.5%, and were the most common cause of death for white babies (ONS 2015a). Consanguineous marriage is the most significant risk factor for CA (Sheridan et al. 2013), and with approximately 60% of marriages reported to be consanguineous in Bradford within the Pakistani population, this risk factor has a large impact (Sheridan et al. 2013). The rate of CA in Bradford has been previously reported at 305.74 per 10,000 live births compared to a national average of 227 per 10,000 nationally (BINOCAR 2014; Sheridan et al. 2013; CDOP 2016).

As well as a high infant mortality rate and rare disease rate, children and families in Bradford have a high level of poverty (Parkin 2012, CDOP 2016).

This resonates with global trends of high CA prevalence usually found in countries or areas with low income (Farmer et al. 2015). Figure 2 presents the percentage of children in Bradford in poor or very poor health by ethnicity compared to the rest of England. Children of South Asian ethnicity in Bradford are in worse health than South Asian children in the rest the UK (Bradford Metropolitan Council 2013).

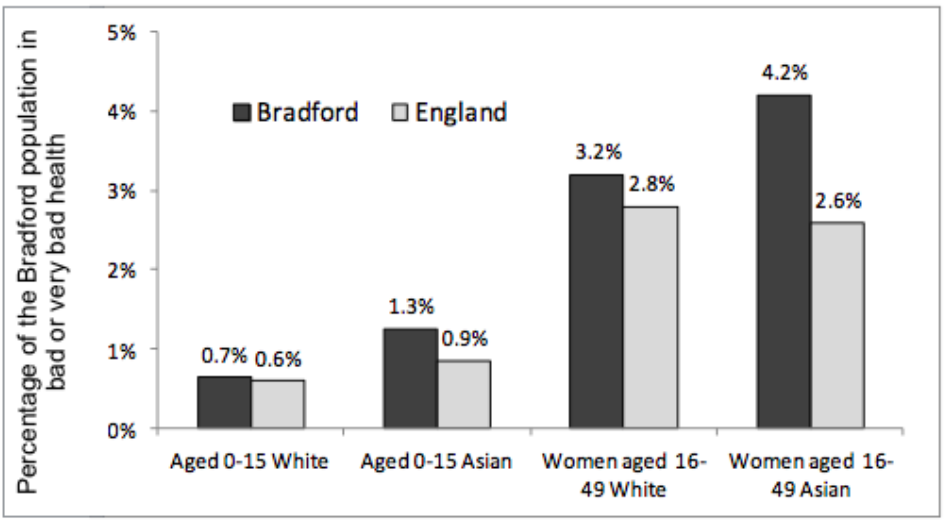


Figure 2: The percentage of the Bradford population in 'bad' or 'very bad' health (ONS 2011, tables DC3201EW)

The high levels of infant mortality, combined with the high number of children with CA living in deprived neighbourhoods in Bradford, creates a group of children whose healthcare needs are likely to be complex. The healthcare use and the different contact points with the healthcare service for these children, together with the impact on healthcare resources, have not been evaluated to date as part of BiB's ongoing research. An evaluation of healthcare use for children with CA is also in high demand in the UK, as CA is a leading cause of infant mortality throughout the UK (ONS 2015a), but there is even more of a demand in Bradford, as the level of CA and consequential childhood disability is among the highest in the UK (Corry 2002; Devereux et al. 2004; Shwarz et al. 2002).

There are some national efforts to investigate service use for children with complex healthcare needs. These point towards a high level of healthcare use for children in Bradford, but they are only preliminary investigations so cannot draw robust conclusions. For example, the National Child and Maternal Health Intelligence Network (PHE 2015) provides some publicly available data on hospital admissions for children aged 0 to 17 years in Bradford. This data shows the number of children with a hospital stay of less than 24 hours in Bradford is very low. Another Bradford study recognised that higher rates of CA increased the demand for antenatal, paediatric and genetic services (Sheridan et al. 2013), but to what extent requires further investigations.

1.4.2 Data linkage

In this thesis, access to primary care and hospital data presents an opportunity for quantifying the impact children with CA have on the healthcare service, by measuring children's contact with healthcare over a specified period of time. BiB linked two sources of routine health data, primary care records and hospital episode statistics (HES), to cohort information in November 2014. This made it possible for BiB researchers to combine detailed socioeconomic information from the cohort participants with clinical information. This provided new opportunities to follow up health outcomes (Wright et al. 2013).

Routine health data is collected from a person's contact with the GP, hospital services, outpatient appointments and prescriptions for medication. It also provides some details on procedures performed during outpatient clinics. Routine health data is valued for its practical, researcher-independent approach to depicting multidisciplinary healthcare use (Bohensky et al. 2010). Linking this data offers a solution when a researcher seeks to examine a comprehensive range of outcomes for comparison, often an important tool in observational research (Bohensky et al. 2010). Data linkage therefore has the utility to describe and quantify healthcare contact points for people with complex healthcare needs (Freeman and Hughes 2010).

These kinds of linkage exercises also provide the opportunity for prevalence studies. Such studies reveal important trends and associations about a population. The Chief Medical Officer (DH 2013b) also endorses such approaches, which link empirical data sources to produce models of good practice in healthcare. The focus on CA provides a study population that requires multiple healthcare professionals spanning a range of services, which may be best investigated using a range of data sources. This approach by no means removes the possibility that children with alternate diagnoses do not have complex healthcare needs. Instead, it allows an exploration of whether multiple routine health data sources prove successful for understanding both prevalence and healthcare use that children with CA accrue.

1.4.3 A model for continual improvement in healthcare

The context of this research within the ongoing BiB study, means the findings and recommendations are aligned with that of BiB which aims to support transformation in the NHS. Findings must therefore be transferrable to clinical, commissioning and research audiences in health. A framework to follow is a sensible place to start when conducting research that aims to make improvements to a complex healthcare system. Epidemiological health needs assessment provides a framework for the kind of information gathering required to bring about change that will be beneficial to the health of the population (Williams and Wright 1998). In order to plan and deliver healthcare services effectively, those responsible, such as commissioners, policy makers and providers, require information about the local population and the current healthcare capacity to meet the population's needs (Turner-Stokes et al. 2013).

The epidemiological health needs assessment invites researchers to consider the way existing services are delivered and the effectiveness and the cost of interventions intended to meet the needs of a population with a specific condition. The epidemiological health needs assessment emphasises that in order for a change to be successful, accurate sources of information, clinical involvement and a close relationship to the planning process are required

(Stevens and Gillam 1998). The epidemiological health needs assessment is a pragmatic and logical approach, as it views researching the impact of ill health and finding strategies to reduce ill health as equally important (Williams and Wright 1998). This approach is referred to when relevant throughout this thesis as a frame of reference to facilitate the applicability of the implications of this study to the healthcare service.

1.5 Aims and objectives

The aims of this thesis are to:

1. Estimate the prevalence of disease attributable to complex conditions in Bradford
2. Quantify the burden these conditions place on the healthcare system and individuals.

The objectives of this thesis are to:

1. Review the epidemiology and healthcare use of children with complex healthcare needs
2. Estimate the prevalence of children with complex healthcare needs using linked datasets
3. Estimate healthcare use of children with complex healthcare needs using linked datasets
4. Discuss the prevalence study and investigation of healthcare use in terms of their implications for improving healthcare services for children with complex healthcare needs.

The structure of Chapter 2 reflects the study objectives. The first part of Chapter 2 addresses the epidemiology and healthcare use of children with complex healthcare needs. It does this by exploring the literature on health system

preparedness, highlighting the barriers and facilitators to coordinated healthcare services, and delineating a definition of children with complex healthcare needs. In order to estimate the prevalence of children with complex healthcare needs, the chapter continues with a consideration of CA data collection as an exemplar population of children with complex healthcare needs, including the case ascertainment methods of CA registers, and alternative approaches using primary care data. To estimate the healthcare use of children with complex healthcare needs, Chapter 2 also explores the different types of routine health data most suitable for measuring and reflecting the healthcare use of children with CA, and the statistical approaches used to analyse routine health data. Throughout Chapter 2, the implications that understanding the prevalence and healthcare use of children with complex needs has for improving healthcare services are discussed.

Chapter 3 begins with a discussion of the philosophy underpinning pragmatic research of this kind, and how pragmatic research approaches that aim to investigate health service delivery are supported by the epidemiological health needs assessment. The subsequent sections detail the strengths and limitations of each data source, and present rationales for the use of two separate but concomitant studies in this thesis. Chapter 3 describes the methods used for study 1 and study 2 separately: study 1, which describes the process of extracting cases of CA from electronic primary care data as an exemplar study population for children with complex healthcare needs, and study 2, which explores the healthcare use of children with CA using standard descriptive statistics and a regression analysis.

Chapter 4 presents the results of study 1 and study 2, including descriptive statistics, regression tables and explanatory figures.

Chapter 5 discusses the results from Chapter 4 in terms of what they add to current research surrounding the impact children with complex healthcare needs have on the health service.

Chapter 6 discusses how the findings might be implemented into healthcare practice, and what aspects of the research require further investigation before implementation may occur.

1.6 Chapter summary

This chapter presents the background for researching children with complex healthcare needs, the proposal for using children with CA as an exemplar of a population of children with complex healthcare needs, and an introduction to the current policy shaping healthcare systems and the delivery of care for children with complex healthcare needs. The specific datasets used to estimate the prevalence of children with CA and their healthcare use are introduced. These include the BiB cohort, which has detailed linkage to sources of routine health data. The epidemiological health needs assessment is outlined, which is used as a frame of reference throughout this thesis to ensure the study implications remain applicable to the planning and delivery of healthcare services.

2 Literature review

2.1 Chapter overview

In Chapter 1, a review of the current healthcare policy shaping children's healthcare services highlighted some barriers and facilitators to coordinated and effective children's care. Poor consensus regarding a definition for children with complex healthcare needs was the first barrier, which was associated with difficulties commissioning services that were capable of appropriately supporting children with these needs. Secondly, a lack of data quantifying access to services was found; such data is essential to help understand whether the supply of healthcare services meets demand (DH 2013b). The facilitators to coordinated and effective care were mainly aspirational policy recommendations outlining improvements for the future. One such recommendation was identifying named healthcare professionals for each child with complex healthcare needs, to assist with streamlining care and reducing unnecessary appointments (DH 2013b).

To answer research objective number 1, outlined in Chapter 1, this literature review explores four main topics. The search strategies for these four topics began broad and systematic, and narrowed in their scope as the research approach became more refined.

Firstly, a broad scoping review of the literature outlining the epidemiology and healthcare use of children with complex healthcare needs is presented. This scoping review also addresses health system preparedness for children with complex healthcare needs, within which are those services that also support children with CA. Key themes are identified and used to structure this scoping review.

Secondly, although there is no single team within the UK healthcare service providing treatment solely for children with CA, there are specific CA disease registers that seek to ensure the appropriate monitoring of CA. This literature

review explores the strengths and weaknesses of the data collection approaches adopted by CA registers.

Thirdly, alternative data collection approaches for CA case ascertainment are explored. These alternative approaches include using secondary data sources such as primary care data, hospital episode statistics and information from patient medical records.

Fourthly, literature that explores analytical approaches to measuring and quantifying healthcare use and an overview of the current, quantitative methods for analysing healthcare data are explored. A search strategy is presented for the initial, broad scoping review, which was detailed and exhaustive, followed by a brief account of those search strategies for the literature presented in the other sections, with links to the appendices for relevant details.

2.2 Review of the epidemiology and healthcare use of children with complex healthcare needs

To understand both the epidemiology and healthcare needs of children with complex healthcare needs, this review takes a holistic approach and looks at literature that considers the perspective of the child and carer, the care team and the healthcare organisation in order to draw a comprehensive conclusion on how best to manage these children's needs (Reid et al. 2005). This comprehensive approach is especially pertinent when aiming to understand how the health system manages complex conditions which are growing in prevalence, require a complex response and coordinated inputs from a wide range of health professionals and services embedded within a system of care (Nolte and McKee 2008).

In this thesis, children with CA can be thought of as the patient-level focus, but an understanding of how the health system supports children with complex healthcare needs in general is required to make recommendations that align

with the health system and organisational-level priorities. These priorities are largely driven by the current clinical approach of assessing children with CA within the UK healthcare system, which, according to local clinical experts, occurs in general children's services, not specific services for CA. Limiting the literature search presented in the first part of this literature review to children with CA would exclude a large proportion of the literature providing a systems and organisational-level understanding of how healthcare services support children with complex healthcare needs.

2.2.1 Search strategy

This is a scoping review, which is an appropriate approach in health research as it draws on information from both healthcare policy and research literature. The main characteristics of a scoping review are that it can provide an overview of a broad topic (Peterson et al. 2017), include a perspective that is applicable to the health service and also aim to identify 'best practice' (Watson et al. 2011). There are key differences between a traditional systematic review and a scoping review. Both start with an inquiry-focused research question, but a scoping review allows for a more general question to be asked and for an exploration of research and healthcare policy literature (Peterson et al. 2017). Because children with complex healthcare needs engage a wide range of services and manifest a wide range of disabilities, a scoping review was deemed an appropriate approach. A scoping review has less depth but a broader conceptual range (Arksey and O'Malley 2007), and, because of this range, a well-executed scoping review provides a richly informed starting point for further investigations (Peterson et al. 2017).

The databases selected for this review were: Medline (In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)), Embase, both accessed via Ovid SP, and CINAHL, accessed via EBSCO, HMIC (Health Management Information Consortium), and Global Health. Search strategies were adapted according to the specific syntax requirements of each database. Search strategies for each database are included in Appendix 1. After conducting the searches, the results

were exported to EndNote X7. All duplicates were identified and removed. Studies were of interest to this scoping review if they reported on service evaluation, service improvement, the experiences of families caring for children with complex care needs, the healthcare use of those children, and the attitudes of healthcare professionals working with them. Both original research studies and reviews – including systematic and narrative reviews – were included, as were studies using attitudinal surveys.

A total of 222 studies were retrieved from database searches, and 36 were retrieved through hand searching of reference lists and using Google Scholar. Studies were initially excluded if they were published more than 10 years ago, which at the time of this search (2015), equated to literature published before 2005. Studies that were not published in English were also excluded. The Preferred Reporting Items for Systematic reviews and Meta Analyses (PRISMA; Moher et al. 2010) was used to guide and organise the selection and exclusion process, as, although this was not a systematic review, this reporting system aids researchers conducting any literature review to follow a methodical and standardised process. A flow chart outlining the selection and exclusion process is included in Appendix 2. A total of 191 articles were then subjected to a more rigorous exclusion process as follows.

The second round of exclusions removed research in the form of poster presentations and conference abstracts, as well as editorials and opinion pieces. Next, all study titles and abstracts were screened for predefined characteristics (Table 1) and studies with relevant abstracts were then subjected to a full text review by the researcher. Further exclusions were made from the full text reviews based on the same exclusion criteria in Table 1. Articles that were included were assessed in terms of their relevance to the aims of the study, their methodological quality, recruitment strategy and their results having implications for the health service. A detailed description of the methodological assessment of the included articles, and reasons for exclusion are included in Appendix 3 and Appendix 4 respectively.

	Include	Exclude
Population	• Children with complex healthcare needs • Children with CA • Children with multiple chronic conditions • Children with complex health needs and disabilities • Children with complex medical needs • Young people with complex healthcare needs	• Focus on a single CA rather than all CA • Survival of children with congenital anomalies • Focus on learning disabilities, not all complex healthcare needs • Adults with disabilities • Parents with complex healthcare needs
Interventions	• Healthcare organisation • Care coordination • Planning children's services • Determine the quality of service provision for children with complex healthcare needs • Economic impact of infants diagnosed with complex healthcare needs on the health service • Factors influencing referrals to specialists • Caring for children with complex healthcare needs at home • Psychological needs of the parents of children with complex healthcare needs • Discharge planning for children with complex healthcare needs • Respite care for children with complex healthcare needs	• Staff specific training • School management rather than healthcare • Service specific rather than the whole care pathway • Focus on implementing one specific intervention

Table 1: Inclusion and exclusion criteria of studies included in scoping review

Following the exclusion process, 75 studies were included. Most studies used qualitative methodologies, such as interviews, surveys and focus groups. One Australian systematic review was found (McCann et al. 2012), and four non-UK cohort studies (Colvin and Bower 2009, Morales-Surez Varela et al. 2009, Wang et al. 2009, Courtwright et al. 2011). The remaining studies were a combination of literature reviews and case studies.

Key themes emerged within these 75 studies. Firstly, 16 studies focused on methods to improve the coordination of care for children with complex healthcare needs within the health service. These methods included examining referral pathways, identifying bottlenecks and reporting on the carer experience of navigating their way through the health service to meet a child's multi-factorial needs. Twenty-three studies explained health system efforts to support parents and carers of children with complex healthcare needs, either aiming to understand the experience of caring for children with complex healthcare needs,

and/or to support carers in their caring role. Twelve studies looked at the utility of named professionals and key workers within the health service for improving the coordination of care for children with complex healthcare needs, and to help improve the efficiency of the referral process. Nine studies explored the health service use of children with complex healthcare needs and health system approaches to help identify children with complex healthcare needs at the earliest possible stage, to ensure the right care is received and the exacerbation of healthcare needs are minimised. A final six studies explored approaches to training within the health service, to help educate healthcare staff on the unique needs of children with complex healthcare needs and improve timely and efficient coordination of care.

The end product of a scoping review is typically a narrative presentation, with minimal or limited statistical information, the intention of which is to synthesise research in the topic chosen and describe the key concepts from a variety of sources (Peterson et al. 2017). The key concepts arising from this scoping review are used as subheadings to structure the layout of the findings. These key concepts are presented in Figure 3.

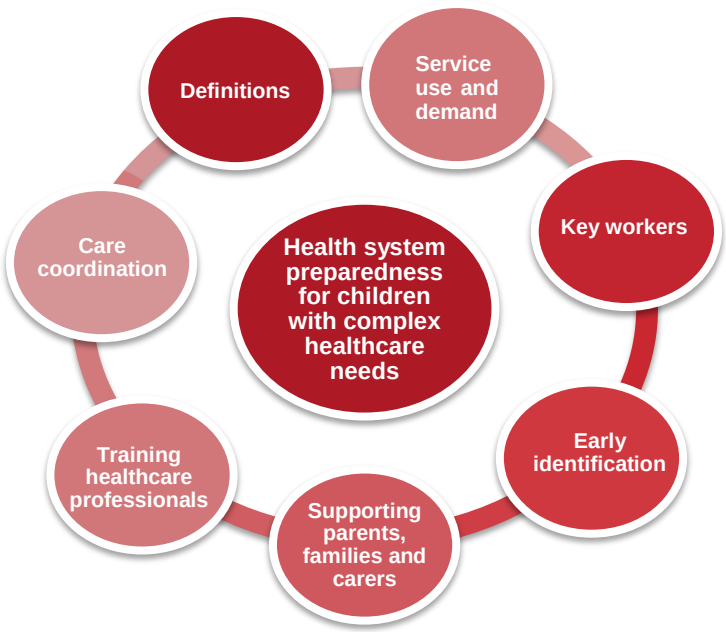


Figure 3: Key themes emerging from scoping review

2.2.2 Definitions of children with complex healthcare needs

Presenting definitions provides clarity at the earliest possible stage of the research (van Mil and Henman 2016), and is important in any discipline. For children with complex healthcare needs, early identification of a definition is especially pertinent as generally this scoping review found poor consensus in the literature on how to define children with complex healthcare needs (DH 2013b). For example, terms such as 'chronic illness', 'disability', and 'chronic conditions', are used frequently and interchangeably in the literature to also describe children with complex healthcare needs (Wang et al. 2009; Hewitt-Taylor 2010; Peter et al. 2011; McCann et al. 2012; Nicholl and Begley 2012; Looman et al. 2013). Interchangeable use of definitions can lead to difficulties when trying to produce focused research, allocating funding for appropriate services for children with complex healthcare needs, and determining the prevalence of complex healthcare needs in the overall population (Burnside, 2012).

Because of the multiplicity of definitions, it has been argued that there should be a focus on a description of the individual, things they do well and independently, and things they require support and assistance with, rather than a specific diagnosis (Baird, 2013). The definition presented earlier in this chapter reflects these support needs, which require services that are specialised, intensive, costly, and requiring a high degree of collaboration between the multidisciplinary team involved in the children's care (Baird, 2013). This definition also implies that making decisions about the care of children with complex healthcare needs will require a minimum of two people, and often a team of professionals acting in conjunction with parents and/or carers. The term 'complex healthcare needs' can therefore be used to describe children with ongoing needs, more than one provider responding to these needs and multiple contacts with the healthcare service (Hefner, 2011). Children's needs should also be regularly reviewed, as some children may only have complex healthcare needs for a certain period of time (McConkey et al. 2007). Addressing a child's

support needs rather than the provision of treatments to meet their medical needs, means the approach to care is consistent with social models of disability and illness, while also linking directly to person-centred care planning (DHSSPS 2007).

There were also some specific care needs identified in the literature that reoccurred as key indicators seen to contribute to a healthcare professional defining a child as having complex healthcare needs. These were technology dependence (Woodgate et al. 2012; Elias et al. 2012; Farasat and Hewitt-Taylor 2007; Hewitt-Taylor 2005; Hobson and Noyes 2011; Kuo et al. 2011; Peter et al. 2011; Nicholl et al. 2013), psychological input and medical input (Watson et al. 2011; Ungar et al. 2014; Colver et al. 2013; Farasat and Hewitt-Taylor 2007; Peter et al. 2011), more than one service provider involved in managing the child's care (Beattie 2000; Brooks et al. 2013; Doyle and Buckley 2012; Hefner 2011; Looman et al. 2013; Kelly et al. 2008; Peter et al. 2011), and an indication of a long-term need for care services (Farasat, Hewitt-Taylor 2007; Carnevale et al. 2008; Hewitt-Taylor 2008b; Wang et al. 2009; Hefner 2011; Watson et al. 2011; Hewitt-Taylor 2012b; Brooks et al. 2013; Colver et al. 2013; Looman et al. 2013; Nicholl et al. 2013; Nicholl and Begley 2012).

While it may be possible to choose one definition and outline the constructs within this definition that make a child complex, some authors stipulate the inevitability of definitions requiring modification, dependent on local demographics, the health system layout, levels of deprivation and ethnic diversity (Wright et al. 2013). For example, in some parts of the UK such as Bradford, there are high rates of child mortality, coupled with high levels of deprivation and cultural diversity. In such areas it may be that more nuanced constructs are required to capture issues like deprivation (Wright et al. 2013). Bradford also has a wide variety of rare and uncategorised conditions (Sheridan et al. 2013), many with differing age at onset. This means that some children with complex healthcare needs take longer to receive a diagnosis than others. This could lead to some children being excluded from receiving treatment if early diagnosis was compulsory for receiving treatment. In order for children

with undiagnosed conditions to receive treatment, more emphasis is placed on choosing a definition that identifies children's functional and psychosocial needs, rather than a medical diagnosis (Baird 2013).

Continuing care is another definition frequently used in the healthcare literature to describe children with complex healthcare needs and the support they require. Continuing care is a term that focuses on the support children need rather than their medical condition (DH 2010). Children with complex healthcare needs can receive continuing care if their support needs can't be met through existing mainstream services or specialist services alone, but not all children with complex healthcare needs will require continuing care (DH 2010). It is essential that children with complex healthcare needs who may require long-term continuing care are recognised and referred to this service at the earliest possible stage (DH 2010). Therefore, continuing care is a type of healthcare support some children with complex healthcare needs will receive, rather than an all-encompassing service.

Most of the studies included in this scoping review provided a definition of children with complex healthcare needs. These definitions were summarised and one definition was chosen that most appropriately complemented the aims of this thesis. The process of selecting this definition involved identifying common constructs within these definitions that identify a child as having complex healthcare needs, a process that is outlined in Appendix 5.

The chosen definition, which was also presented in the introduction of this thesis, is as follows:

> 'The child has severe or profound disabilities in at least three of the following categories or the child has severe or profound disabilities in at least two of the following disability categories plus need at least two types of resources. In either case the impairments and needs of these children

are sustained lasting for more than six months and ongoing' (DHSSPS 2007: 24).

Disability categories

- Motor impairment
- Hearing impairment
- Visual impairment
- Cognitive impairment
- Speech and language impairment
- Behaviour problems
- Feeding problems
- Additional chronic health needs

Resource types

- Therapy services
- Additional educational resources
- Nursing care needs
- Social care resources
- Mental health services

2.2.3 Care coordination

The Agency for Health Research and Quality (2014) defines care coordination as:

'deliberately organising patient care activities and sharing information among all of the participants concerned with a patients care to achieve safer and more effective care. This means the patients' needs and preferences are known ahead of time and communicated at the right time to the right people, and this information is used to provide safe, appropriate, and effective care to the patient' (Agency for Health Research and Quality 2014: 1).

Timely collaboration and care coordination are therefore essential if patients are to receive the best possible care. However, many authors recognise that children with complex healthcare needs have continued to be identified as being the most fragile, most challenging to manage, and of greatest concern to the healthcare sector (DH 2013b, Berry et al. 2015; Kuo et al. 2011). Children with complex healthcare needs are at risk of facing further complexities as a result of uncoordinated responses to each of their problems (DH 2013b).

Successful coordination requires solid support structures between partner organisations, agreement and direction at policy level, and strong communication platforms between healthcare professionals and families to achieve competent care delivery (Kingsnorth et al. 2013). Other authors suggest successful coordination may require the support of healthcare commissioners and primary care trusts, linked with local authorities, education and social services (Watson et al. 2002, Law et al. 2011, Bachmann et al. 2009, Pratt et al. 2012, Brooks et al. 2013).

Some authors report that there appears to be more of an emphasis on the design of new children's services rather than evaluation of the old that might help to understand what successful coordination looks like (Watson et al. 2011, Clarke 2011, Colver et al. 2013, Kirk 2008). Colver et al. (2013) noticed a lack of evaluation for health services providing care for specific conditions, such as diabetes, cerebral palsy and autism spectrum disorder. Poor communication between healthcare staff in hospitals and the community is a common barrier to effective coordination. Other barriers included a lack of funding for specialist equipment, inexperienced staff and complicated legal liability issues. Consequently, parents are often left to manage coordination of their child's care (Watson et al. 2002, Dale and Godsman 2000). This can be very time and energy consuming and can result in parents experiencing social exclusion (Watson et al. 2002, Dale and Godsman 2000).

Providing inadequate care coordination can lead to serious patient safety issues, as patients can be harmed during periods of service transition or

referral. The Royal College of Physicians (2015) recommends that ensuring patients are not harmed during the coordination of their care, requires systems to be designed to facilitate collaboration through information sharing and allowing time for communication among clinicians. As expressed by the Royal College of Physicians (2015), prioritising communication with colleagues over the immediate pressures of discharge and treating patients may seem unlikely within the current, overstretched healthcare budget. There are, however, recommended ways to improve coordination without allocating additional funding. One of these is to use routine health data to monitor the performance of multidisciplinary teams, tracking and monitoring patients and capturing staff interventions (Royal College of Physicians 2015).

Children with complex healthcare needs are also known to experience poor outcomes in transitional care. Transitional care is the move of young people with physical and medical conditions from children's to adult services, and is a landmark moment in the coordination process and the families and children's lives (Royal College of Nursing 2013). Poor transitions can further complicate care and are recognised in the literature to lead to communication issues between the healthcare provider and the parents/carers, failure to attend outpatient appointments, increased rates of emergency admissions, disease complications, and long-term health and social problems (Catlin et al. 2008, Aite et al. 2013, Dale and Godsman 2000, Elias et al. 2012, Colver et al. 2013, Watson et al. 2011, Watson et al. 2002). Also, the economic costs of an unsuccessful transition from childhood to adult healthcare services are reportedly very high compared to current levels of public expenditure for disabled children (Knapp et al. 2008). Hewitt-Taylor (2012b) added that allocating funding to younger children, which then ceases when children move to adult services, is a very poor use of resources. Resources must be distributed across age groups as well as being dependent on individual needs, and planned in such a way that the family are considered and included throughout (Hewitt-Taylor 2012b, Tait 2002).

Good practice incentives can be drawn from other healthcare teams across the UK to benchmark best practice. For example, Tower Hamlets, which is one of the London Boroughs has 37.8 children per 1,000 births living in poverty (higher than Bradford at 23.9 per 1,000 births), and, as a result, local councils have set up a Children with Disabilities team that provides link coordinators, transition workers and a practical directory for carers, parents and professionals to help navigate the system (Tower Hamlets Council 2017). Tower Hamlets Council specifies on their website that there is a difference in service provision between universal services for children, including maternity services, health visiting and children's centres, and the targeted specialist services required for children with complex healthcare needs (Tower Hamlets Council 2017). Birmingham, a city with higher rates of early childhood mortality than Bradford (PHE 2015), has a programme implemented by local councils that supports the co-development of care plans between education, health and social care services for children with complex healthcare needs (Birmingham City Council 2015). This collaborative approach to providing care has the combined aim of providing effective care and also enabling services to better coordinate support and provide families with a single point of contact (Birmingham City Council 2015). While there are some examples of good practice, evaluation of these kinds of services are lacking, so it is not known how effective they are.

2.2.4 Key workers

Caring for a child with complex healthcare needs throws the family into a new and unfamiliar world (Howitt 2010). Howitt (2010) explains that having someone to help navigate the unfamiliarity of being a carer, can also help them to understand the difference between coping and desperation, as well as managing care safely at home. The Royal College of Paediatrics and Child Health (2014) and the Chief Medical Officer (2013b) recommend that identifying key workers such as named GPs or nurse coordinators would be a fundamental step towards improving the coordination of children's care. Mengoni et al. (2014) highlights that key workers, or people that carry out key working functions, may have been given a number of titles, including care coordinator,

lead professional, link worker, family support worker, service navigator and family liaison, and, while recognising this range of language, key worker will be referred to throughout this thesis for consistency. Key workers and the role they provide can be defined as a set of functions that enable an integrated approach to supporting children, families and carers (Mengoni et al. 2014). These functions might include emotional and practical support (care coordination, planning and assessment), as well as information and specialist support (Mengoni et al. 2014).

Some authors describe key workers as healthcare professionals with the ability to provide a single point of contact for all the healthcare services required to meet the needs of each child. Such a person requires a mix of skills in order to communicate and understand the psychosocial, financial and medical needs of a child (Looman et al. 2013, Tait 2002, Pratt et al. 2012, Brombley 2008, Farasat and Hewitt-Taylor 2007). Some authors recommend that flexibility of roles may help transfer focus away from needs being met by a specific profession. Including the needs of the whole family is also recommended (DH 2009, Law et al. 2011, Hewitt-Taylor, 2005). Providing a consistent training package for key workers across disciplines may also help healthcare teams understand the diversity of the key worker role, while simultaneously helping professionals understand how a key worker might fit into a multidisciplinary team (Garland et al. 2001; Áskelsdóttir et al. 2008; Brombley 2008; Beattie 2000, Pratt et al. 2012; Tan et al. 2012; Looman et al. 2013).

Despite healthcare policy recommending and outlining the core elements of the key worker role, the realities of how they might work in practice lack standardisation and depend on a considerable number of factors that have not been subjected to service evaluation (Garland et al. 2001, Áskelsdóttir et al. 2008, Brombley 2008, Beattie 2000, Pratt et al. 2012, Tan et al. 2012, Looman et al. 2013, Hillis et al. 2016).

Key working is not a new concept, as Beattie (2000) explains. People carrying out such a role have been reported in the literature for many years. Their

presence can reduce the need for parents to ‘tell their tale’ many times, as well as ensure clarity of professional roles and avoid crossovers for both parents and professionals (Beattie 2000). The Children and Families Act (The Stationery Office 2014), the Code of Practice for working with children and young people with Special Educational Needs and Disability (Department for Education 2014b), and the Chief Medical Officer (2013b) have created a renewed driver for change, as they all place an emphasis on joined up working between education, health and social care services, with key working being one of the vital methods for helping services achieve this (Mengoni et al. 2014).

Child passports are a later addition to key worker research. It has been suggested that they assist with the navigation of multiple healthcare services and act as a tool for the key worker (DH 2013b). Child passports are records that include information about the child’s condition and their care needs, with the aim of preventing the need for repeated assessments each time the child visits a different healthcare service (DH 2013b). Child passports are considered a marker of good practice as they assist key workers with coordination, using shared communication across the various services a child requires without necessarily requiring increased staff resources (Law et al. 2011).

Some authors argue case management approaches using key workers can reduce the time spent explaining the child’s medical needs to multiple professionals, and release more time that can be spent on rehabilitation needs (Brombley 2008; Pratt et al. 2012). In this way, key workers are placed in an advantageous position, where they can oversee the child’s rehabilitation, providing regular review and outcome measurement and helping to identify and adapt interventions over a child’s illness trajectory (Brombley 2008; Pratt et al. 2012). Tan et al. (2012) suggests that the familiarity and rapport that results from the support of a regular key worker may also help to support families who are unfortunate enough to experience the death of their child.

Key workers already work well in other areas of healthcare, and good practice examples from these can be benchmarked against services for children with

complex healthcare needs. For example, the DH (2013a) highlights that community nursing services, who work with a range of different professionals, are an ideal profession to fit the role of a key worker, as they are trained to balance medical needs alongside an emotional and empathetic role (Garland et al. 2001). In older people's services, experienced community nurses, otherwise known as community matrons, work closely with patients in community settings and use case management and regular reviews for older people with multiple long-term conditions, high risk of falls, poor social circumstances, and multiple medications (NHS England 2015). Multidisciplinary teams called intermediate care teams are another example of an NHS team of health and social care staff working together, in this case to prevent hospital admissions and facilitate timely hospital discharges (NHS England 2015). Intermediate care teams also have a named GP or geriatrician, with the most complex cases led by a senior clinician.

Several authors suggest that the distance patients live from hospital can further complicate communication between healthcare services and the patient, whereas proximity can increase successful communication (Manhas and Mitchell 2009, Law et al. 2011). Therefore, key workers also need to be prepared for children who live considerable distances from healthcare services requiring extra attention to ensure they receive optimal care.

2.2.5 Service use and demand

Children with complex healthcare needs place considerable demands on healthcare systems. They are likely to make multiple transitions across providers and care settings and are at high risk of hospitalisation and re-hospitalisation throughout their childhood (Cohen et al. 2012). Such frequent contact with the healthcare service is reported to be both distressing and disrupting for families and children. There are some services that are not only in high demand but also in short supply. These include respite services and the provision of specialist equipment. Many authors recognise how difficult respite services are to access (DH 2013b, Law et al. 2011, Franck 2004, Thurgate

2005, Whiting 2013, Whiting 2014). The availability of these services, has historically been inconsistent and largely dependent on the child's diagnosis, with some children determined to be ineligible to receive this service (Whiting 2013).

As well as direct healthcare costs, in the form of the provision of medical care, there are indirect and associated costs of caring for children with complex healthcare needs. These are difficult to identify and quantify (Cohen et al. 2012). A total 175,000 parents have reported that they stopped employment in order to stay at home and look after a child with medically complex healthcare needs, and 5% of families with the most medically complex healthcare needs reported at least five unmet medical needs (Kuo et al. 2011). Stabile & Allin (2012) report that having a child with disabilities increases the likelihood that mothers (and less often fathers) will either reduce their working hours, or stop working altogether. Furthermore, the shift of care from hospital to home has blurred the boundaries between formal and informal care, inadvertently increasing the number of 'expert carers' (McDonald et al. 2016). Expert carers are family members who have to learn technical health procedures such as peg feeding, intravenous therapy, dialysis or ventilation care, just to manage their child's condition at home (McDonald et al. 2016).

Some research suggests that the uptake of healthcare services and informal care differ dependent on ethnicity and that caregivers from ethnic minority backgrounds are sometimes less likely to access health services (Magana and Smith 2008). Reasons identified included language barriers and differences in education levels (Magana and Smith 2008). Magna and Smith (2008) advise that due to large differences in health behaviours and access to care between different ethnic groups, care providers need to consider differing trends across ethnicities when designing care programmes.

The severity of the child's condition has also been linked to the strain placed on the family – as the complexity of care increases, the necessity for specialist equipment and complex care increases (Brooks et al. 2013, Franck 2004). One

study identified that children with complex healthcare needs living at home required on average 22 pieces of equipment per child – mobilisation and elimination equipment being the most commonly prescribed (Nicholl et al. 2013). Having medical equipment in a home is described to be disruptive and it can also have a negative impact on wellbeing, leaving families and carers with feelings of unease when operating specialist equipment without adequate training (Brooks et al. 2013, Nicholl et al. 2013, Peter et al. 2011).

Being technology dependent can also cause delays in discharge from hospital to home, even when the child may otherwise be medically stable, as equipment is often in short supply (Lenton et al. 2004). Medication lists for children are known to be long and frequently changing, which can influence the number of medication errors and result in potential illnesses (Shiviani et al. 2012). However, electronic medical records, key workers and good communication have all been identified as solutions to help prevent medication errors and ensure consistent decision making (Abbass et al. 2012). Similarities can be drawn to children who require palliative care, which involves tending to the families and the child's needs equally, managing the multidisciplinary teams involved in the child's care and providing the best medical care available (Jones et al. 2013).

2.2.6 Early identification of complex healthcare needs

The Chief Medical Officer (DH 2013b) advocated for the early identification of all childhood diseases, which is most often achieved when staff are well trained and supported by a clear service model. Early identification is essential to reduce the impact on other healthcare services (Mengoni et al. 2014). However, early identification also requires forward planning, which does not always happen in practice (Aite et al. 2013). Poor communication between parents, the diagnosing clinician, and medical centres is one such barrier to the early identification of childhood diseases. Poor communication is linked with poor coordination and delays to referrals that initiate the next steps of the child's care, as well as creating anxiety for parents, which can contribute to poor

experiences of care (Áskelsdóttir et al. 2008, Aite et al. 2013, Watson et al. 2011). It is suggested that having a definition and consequently improved consensus regarding the classification of children with complex healthcare needs could be key in helping facilitate early detection, coordination and management of children's care when admitted to hospital (Colvin and Bower 2009, Farel et al. 2003).

Communities with high levels of deprivation and ethnic diversity should also be given special attention regarding early interventions and preparing healthcare systems for complex healthcare needs, as these communities are reported to have worse health outcomes (Kurinczuk et al. 2010, Wright et al. 2013). There are also more specific patient characteristics that may be better indicators of the need for complex care. For example, Bettge et al. (2014) observed that children born with lower birth weights were linked to higher rates of special educational needs and low socioeconomic status, Morales-Surez Varela et al. (2009) noted an association between socioeconomic status and the prevalence of CA, and Wang et al. (2009) found that low socioeconomic status was related to worse outcomes for children with complex conditions even when there was the same level of access to healthcare across socioeconomic groups (Wang et al. 2009).

2.2.7 Supporting parents, families and carers

Stress and emotional pressures are often experienced by the parents and carers of children with complex healthcare needs, and consequently are the subject of much research (Bonanno et al. 2013, Hewitt-Taylor 2009, McCann et al. 2012; Narramore 2008; Whiting 2014; Hewitt-Taylor 2009, Fonseca et al. 2014; Kirk and Glendinning 2002; Runciman and McIntosh 2003; Nicholl and Begley 2012). The prevalence of maternal depression is reported to be highest in parents who care for a chronically ill family member (Sills et al. 2007). To avoid parental and carer burnout, some research suggests the impact of caregiving on parents should be addressed appropriately and at the earliest possible stage (Hewitt-Taylor 2009). Some amelioration of stress can be achieved by providing timely advice, talking parents though care plans and

providing counselling when required (Fonesca et al. 2014). Solutions such as these may be especially valuable to parents who find the caring role challenging, and may reduce the risk of poor mental health, which if left untreated may negatively affect the child (Fonseca et al. 2014, Narramore 2008).

Fathers are reported to be increasingly involved in substantial amounts of technical and nursing care (Hobson and Noyes 2011; Bonanno et al. 2013). Establishing how the caring role will be divided between parents is essential, but health professionals should ensure that they are prepared to provide tailored advice for supporting the resilience of fathers as well as mothers (Hobson and Noyes 2011; Bonanno et al. 2013). Understanding what caring means to each family member, as well as how caring roles merge, is essential in establishing effective therapeutic rapport (Hewitt-Taylor 2008b; Hewitt-Taylor 2009, Kirk and Glendinning 2002, Hewitt-Taylor 2008a).

Following interviews with parents of children with complex healthcare needs, Whiting (2013) reported that parental experiences of caring were fairly consistent regardless of the specific diagnosis or medical need. Some of the most common conditions placing pressure on the relationship between parents and their child were life-limiting conditions and technology dependence (Whiting 2013). As specialist equipment is commonly prescribed for children with complex healthcare needs, several authors suggest equipment training for parents and carers is an essential first step (Runciman and McIntosh 2003; Nicholl and Begley 2012). Families with higher technical requirements are also more likely to report unmet needs, as technology and equipment is generally under-resourced (Brooks et al. 2013; Franck 2004; Hewitt-Taylor 2005), along with respite care (DH 2013b; Law et al. 2011; Franck 2004; Thurgate 2005; Whiting 2013; Whiting 2014).

Two authors report that parents find it easy to lose trust with health professionals if they receive poor information or advice, or if professionals are perceived to be struggling to understand their child's needs (Dybwik et al. 2011;

Whiting 2013). Easy access to information and advice was valued by parents; examples include practical help with finances and peer support interventions, such as blogs and community groups (Kirk and Glendinning 2002; Whiting 2013; Nicholl and Begley 2012). Being able to hear stories from parents in a similar situation equipped parents with the knowledge that they were not struggling alone. When this, combined with examples from those managing their child's care well, provided parents with hope for the future and reduced feelings of loneliness were reported (Kirk and Glendinning 2002; Whiting 2013; Nicholl and Begley 2012).

2.2.8 Approaches to training health professionals

Staff training in care for children with complex healthcare needs can enhance staff confidence and assertiveness, and can be provided in addition to their more practically based professional training (Dale and Godsman 2000, Elias et al. 2012). One of the challenges reported by staff working in teams providing care for children with complex healthcare needs is workload (Furness et al. 2009). Healthcare staff report that trying to care for children with complex healthcare needs, combined with insufficient time and training in a busy acute environment, is unsustainable as well as being frustrating (Furness et al. 2009). Additional training is understood as an essential step towards equipping staff with the skills to respond to pressures from parents who are desperately seeking a solution for their child's care (Dale and Godsman 2000, Elias et al. 2012). Some authors suggest that establishing a clearly defined pathway of care and specifying the healthcare professionals' roles within this, may strengthen the emotional resilience of staff (Dale, Godsman 2000, Elias et al. 2012).

Some researchers state that skill sharing and joint working to promote the flexibility of healthcare roles should be an automatic feature of healthcare teams, and should be maintained through joint staff training (DH 2009, Law et al. 2011, Hewitt-Taylor, 2005a). Looman et al. (2013) suggest that encouraging professional roles to be flexible may also help prevent imbalances between the

medical or technical aspects of caring for children with complex healthcare needs, and the psychosocial aspects of care (Gangadharan et al. 2001; Looman et al. 2013). Hewitt-Taylor (2005a) adds that the flexibility of roles is especially pertinent in teams providing services for children whose healthcare needs span several specialisms. In these circumstances, healthcare teams need to have at the very least an understanding of each specialism to help coordinate care (Hewitt-Taylor 2005a). Joint working and flexibility of roles should not lead to an erosion of core skills (Hewitt-Taylor 2012a). Shared posts between complex care teams and mainstream services are one option to ensure the needs of the child are met over the long term (Hewitt-Taylor 2012a). Distance learning or in-service training provided by key workers with previous experience of managing caseloads of children with complex healthcare needs is another suggestion (Hewitt-Taylor 2012a).

2.2.9 Summary of literature exploring health system responsiveness

This scoping review has presented and summarised literature from both healthcare policy and research. It has covered seven main themes, which capture challenging yet essential elements of successful health system management for children with complex healthcare needs. These themes were: definitions of children with complex healthcare needs; care coordination; key workers; service use and demand; early identification of complex healthcare needs; supporting parents, families and carers; and approaches to training healthcare professionals. These themes are also interrelated. Together they identify objectives for a healthcare system that must be managed in synergy in order to support children with complex healthcare needs efficiently and effectively. Poor coordination of care can lead to delays in early identification of a child's healthcare needs, and can be improved using identified named professionals, training of healthcare staff and surveillance of patients using routine health data and technology.

Key findings included the following. An appropriate definition of children with complex healthcare needs should promote a focus on the child's support needs

rather than their medical conditions (McConkey et al. 2007; DHSSPS 2007). Providing and reporting a consistent definition of children with complex healthcare needs at an early stage is an essential component in understanding and identifying children with complex healthcare needs, so they can receive the right care at the earliest possible stage. To maintain successful care coordination for children with complex healthcare needs, understanding their needs in depth is suggested to be the essential first step (Fonseca et al. 2014; Narramore, 2008). Doing this will enable shortcomings in services that support them to be addressed (Fonseca et al. 2014; Narramore, 2008). Those services that have managed to provide good support involve close liaison with commissioning and management, with clearly defined pathways that support accurate referrals to different teams (Watson et al. 2002; Law et al. 2011; Bachmann et al. 2009; Pratt et al. 2012; Brooks et al. 2013). Close liaison and clear pathways are also reported to help prevent overuse of services that are already in high demand (Dale and Godsman 2000, Elias et al. 2012). The role of key workers is frequently addressed in the literature included in this scoping review. How the role the key worker model might work in practice, and whether it will improve the efficiency of care coordination, remains unclear (DH 2013b).

There is a logical ordering to follow when addressing the seven themes identified in this scoping review. Before investing time and resources into healthcare improvements, there needs to be evidence that there is a reason to do so. Fonseca et al. (2014) and Narramore (2008) remind us that understanding a child's healthcare needs in depth is the first step towards improving care for children with complex healthcare needs, and it is only then that the extent to which services require redesign, healthcare staff require training and families require supporting is revealed. This detailed level of understanding can be ascertained via longitudinal data analysis and a detailed review of routine health data. Routine health data has the level of granularity required to help equip healthcare decision makers with quantitative evidence of healthcare use (DH 2012; DH 2013b).

Quantifying the frequency and demand of the services supporting children with complex healthcare needs remains under researched (DH 2013b). The Children and Young Peoples Outcomes Forum (DH 2012) confirms a lack of quantitative analyses for children with long-term conditions, disabilities and palliative care needs, and recommends high-quality studies using existing healthcare data to better quantify and understand the healthcare use of these children.

As this scoping review has highlighted, there are many childhood conditions that can be considered complex, covering a wide range of healthcare services, making data collection unfocused and difficult. Firstly, a specific and representative study population of children with complex healthcare needs is required. As mentioned in Chapter 1, CA forms the study population in this thesis, as CA typifies the kind of complexity experienced from a range of disabling conditions. Secondly, to gain a health systems perspective of these children's needs, healthcare use will need to be captured across a range of services. Once these steps have been addressed, the literature from this scoping review can ensure the findings are aligned with priorities for health system preparedness.

2.3 Congenital anomaly data collection using registers and routine health data

As introduced in Section 1.4.2, routine health data (including primary care data) was linked to the BiB cohort, making it possible to explore new associations between healthcare use and the socioeconomic information from the cohort participants. In this section, the strengths and weaknesses of CA registers for CA case ascertainment, and the validity of primary care data for CA case ascertainment, are explored. To do this, the following search strategy was implemented. The Ovid database was searched using the terms "primary care" AND "congenital anomalies" with relevant synonyms. Searches were filtered to human studies and had no date restrictions. The first search returned 13 relevant articles reporting the use of primary care databases for CA case

ascertainment, of which seven were methodologically sound. Papers were excluded if they were too condition specific, or based on small numbers. The inclusion and exclusion criteria can be found in Appendix 6. A web-based search was performed to identify the relevant websites to describe the design and data collection methods of CA registers in the UK.

2.3.1 Congenital anomaly registers

In order to collect data on children with CA, CA registers provide an information and resource centre for new research relating to risks factors associated with CA, or geographical clusters of CA prevalence (BINOCAR 2014). CA registers record children diagnosed with a CA in hospital and assign them into groups depending on the severity of the CA and the human body system each CA affects. Because of the debilitating impact of CA on children's health, CA registers were established to perform epidemiologic surveillance of CA, not just in the UK but also worldwide. Although there is no legal requirement for CA notifications, failing to understand the impact CA has on the healthcare service is likely to cause poor and unequal healthcare provision. CA notifications are not only important for accurate prevalence estimates but also for healthcare planning (Misra et al. 2005).

The British Isles Network of Congenital Anomaly Researchers (BINOCAR 2014), which was the main CA register in the UK and the Republic of Ireland, has now been replaced by PHE and the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS; 2015). Until the existence of NCARDRS, which is still in the early stages of CA data collection, only 49% of births were monitored for diagnoses of CA by seven regional registers in the UK, and each register was slightly different in its data collection strategies. This made it difficult to provide comprehensive outcome data for CA screening programmes in the UK (PHE 2014).

Both BINOCAR and NCARDRS follow guidance on the registration, classification and severity of CA from the European Surveillance of Congenital

Anomalies (EUROCAT 2013). EUROCAT (2013) provides the CA coding and classification for all CA registers in Europe, helping to standardise clinical diagnoses and creating data that can be analysed for surveillance and research purposes. EUROCAT (2013) coordinates the European network of population-based registers, which covers around 30% of the European Union birth population as well as some non-EU countries with a total 43 registers in 23 countries (Boyle et al. 2017). CA registered with EUROCAT (2013) includes those diagnosed from live births, foetal deaths from 20 weeks' gestation, stillbirths and terminations of pregnancy for foetal CA (Boyle et al. 2017). This kind of classification system is imperative for grouping together CA with similar aetiological or clinical features and was used in this thesis to standardise the coding of the primary care data extraction.

EUROCAT (2013) categorises and codes CA into bodily system groups, for which prevalence information is routinely produced. These subgroups have been defined based on those that show relative health impact in different organ systems, as well as being relevant to health service provision. They are also organised in terms of conditions that are consistently diagnosed across Europe, and are of reasonable frequency so that yearly prevalence calculations can be meaningful (EUROCAT 2012). Using a standardised and organised diagnosis system, makes it possible to compare the findings of CA prevalence with both national and European prevalence estimates and also explore whether children with more severe CA are associated with greater healthcare use.

2.3.2 CA case ascertainment following national guidelines

The rate of CA previously reported in Bradford was 306 per 10,000 live births (Sheridan et al. 2013), which, at the time of discovery, was higher than the national average of 227 per 10,000 live births (BINOCAR 2014; Sheridan et al. 2013; CDOP 2016). The data collection methods in this previous CA study, which will be referred to as phase 1 (Sheridan et al. 2013) henceforth, mirrored that of national and European CA guidelines outlined in the previous section (2.3.1). BINOCAR (2014) and EUROCAT (2012), state that 98% of CA cases

used to calculate CA prevalence are diagnosed at age one year. The guidance surrounding the appropriate age range for CA case ascertainment carries some uncertainties. BINOCAR (2014) states that although 'most' CA are notified either in the antenatal period or soon after birth, later CA diagnoses, if found, are welcomed.

Despite this statement, BINOCAR (2014) further adds that very few CA diagnoses are registered in the postnatal period, and only 2% after the age of one. Despite this, of the 36 CA registers in Europe, seven reported more than 2% of CA cases were diagnosed after age one. These later registrations amounted to between 5–10% of total CA registrations (Greenlees and Garne 2009). There is also some speculation that these figures are further underestimated due to inconsistencies in the definitions and data variables between different CA registers, and an absence of follow-up data (Boyd et al. 2005; Charlton et al. 2010; Scheuerle et al. 2009; Garne et al. 2011; Loane at al 2011).

2.3.3 CA case ascertainment using primary care data

Because of the uncertainties surrounding CA prevalence from registers, alternative approaches to case ascertainment using longitudinal data are being explored by researchers. Two studies using the THIN primary care database (2017) identified higher numbers of CA diagnoses than national figures reported by EUROCAT (2013) (Sokal et al. 2013; Sokal et al. 2014). Sokal et al. (2013) compared the number of CA cases recorded in the THIN (2017) primary care database up to the child's first birthday to the number of CA cases over the study period of 6.7 years (Sokal et al. 2013). The CAs recorded up to the child's first birthday amounted to a prevalence of 198 per 10,000 live births, higher than the prevalence reported by EUROCAT (2012) at the time of 167 per 10,000 live births. When including CA cases up to age 6.7 years, the prevalence increased to 277 per 10,000 live births, meaning age at diagnosis was an important explanatory variable for increased prevalence (Sokal et al. 2013).

To ensure the additional CA diagnoses picked up using primary care data are valid cases, and are not the result of electronic coding errors, several studies compare diagnoses made in primary care databases to the paper medical records consultants use to record CA diagnoses (Wurst et al. 2007a; Devine et al. 2008; Charlton et al. 2010; Hammad et al. 2013). While most of these studies find that primary care data records the same CA diagnoses as those made by the GP or consultants, ranging from 71% (Devine et al. 2008) to 93% agreement (Hammad et al. 2013), additional caveats are uncovered, which require addressing.

These caveats include discrepancies in the dates of diagnosis, which in one study were found to be less reliable in the primary care record than the original diagnosis date made by the GP (Hammad et al. 2013). Only 58% of CA diagnosis dates identified using primary care data agreed with the GP's date of diagnosis. Diagnosis dates tended to be later in primary care data than the date reported by the GP, yet, of those dates that were different, almost a third were within 30 days of the GP's reported date. Patients, who remained with the same GP practice were more likely to have accurate dates of diagnosis; a finding similar to another study comparing CA case ascertainment from electronic medical records to GP diagnoses (Wurst et al. 2007a). Another study suggests that the first definitive CA diagnosis may be in the form of a letter from a specialist, and the diagnostic code is only recorded in the GP system when a drug is prescribed for that condition, delaying diagnosis dates in primary care data (Nicholson et al. 2013).

Bohensky et al. (2010) makes the point that although data linkage in research studies has increased almost six fold in the last 20 years, and is a very important tool for enhancing the detail of observational data, it may be associated with various types of error if the process for linkage is not outlined clearly. Sometimes, some variables are more complete than others when performing data linkage. To account for missing data when performing data linkage, it is advised that researchers either merge in other datasets that have

more complete information on the variables with missing information, or perform multiple imputation using chained equations (HQIP 2017). To make this decision, it is strongly advised that denominators used for linkage are reported, and the characteristics of the missing information are measured and reported (Bohensky et al. 2010).

These previous studies suggest that primary care data may serve as a valid source of CA case ascertainment, as well as a valid data source for picking up additional CA cases diagnosed after the age of one. At the same time, the expected study period should be extended to ensure late diagnosis/data migration is accounted for (Hammad et al. 2013).

2.4 Measuring healthcare use for children with CA

To identify appropriate literature exploring approaches that aim to measure and quantify the healthcare use and impact of children with complex healthcare needs (and within that children with CA) on the healthcare service, the following search strategy was implemented. The Ovid, PubMed, Ethos, OpenGrey and greylit databases were searched using key terms “congenital anomalies” AND “healthcare use”, with relevant synonyms. The searches combined returned 42 relevant articles. Results were excluded if they reviewed healthcare use in relation to one specific condition, or one particular medical intervention, rather than healthcare use in general. The results included cohort studies (n=13), cross sectional reports (n=15) and good practice reviews (n=14) relating to care coordination, management and efficiency models applied to primary or secondary care. To identify information relating to the current primary care databases in the UK, a web-based search was performed, and information was extracted from the relevant primary care database web pages.

2.4.1 Current approaches in healthcare

Although primary care services play an important role in helping prevent hospital admissions for children with CA (Colvin and Bower 2009; Grosse et al.

2009), the need and demand for primary care services are intensified by patient complexity, levels of deprivation and primary care practice provision (The Kings Fund 2016b). This means that the complex healthcare needs of children with CA requires the support of a wide range of healthcare services. To represent the multidisciplinary care needs of children with CA, it has been suggested that a combination of primary care consultations, hospital services, the types of conditions children are diagnosed with, prescribed medications, and referral information produce the best estimates of healthcare use (Crooks et al. 2015; Dawson et al. 2013; Pasquali et al. 2014).

Of those studies that measure the healthcare use for children with CA, most report an increase in demand for healthcare. There is general agreement in the literature that hospital use for children with CA increases compared to children without CA (Lindower et al. 1999; Colvin and Bower 2009; Polita et al. 2013; Dawson et al. 2013; Simeone et al. 2014; Faraoni et al. 2016; Simeone et al. 2015; Agarwal et al. 2016; Cedars et al. 2016; Islam et al. 2016). Increases in admissions and prolonged hospital stays for children with cardiac CA were also associated with increased hospital costs (Petersen et al. 2013; Pasquali et al. 2014; Simeone et al. 2014; Simeone et al. 2015; Faraoni et al. 2016; Agarwal et al. 2016; Dawson et al. 2013; Islam et al. 2016). Two studies in particular found that surgery and readmission rates for children admitted to hospital for cardiac CA placed considerable demands on resources (Cedars et al. 2016).

Large differences have also been reported between the total time spent in hospital for children with and without CA. While an average of 1.5 admissions and 3.4 days in hospital have been estimated for children in England in the first two years of life (Fitzsimons et al. 2013), children with multiple CAs were estimated to experience twice as many admissions and two to three times as long in hospital compared to children without CA (Fitzsimons et al. 2013). One study reported elective surgery was the most common reason for admission to hospital for children with CA (Polita et al. 2013). Length of stay following surgery for children with CA was found to vary significantly within a single neonatal unit in one study (Shetty et al. 2016). No studies that combined primary care data,

HES data, and referrals to specialists in order to present a more detailed picture of the healthcare needs of children with CA were found.

Other factors aside from ill health are known to affect healthcare use. Diversity and deprivation are also recognised as a causative factor of primary care pressures (The Kings Fund 2016b), as well as variations in primary care practice provision (Kelly et al. 2016b). This insight is referred to as 'the inverse care law' (Hart 1971). Healthcare provision for children is known to suffer disproportionately from the effects of poverty (Marmot 2010). Those most in need of healthcare are often those who are most likely not to be offered it. Addressing the inverse care law is a key priority for NHS commissioning (Marmot 2010; The Kings Fund 2015). It remains necessary, therefore, to understand how levels of material deprivation affect healthcare access and use for children with CA. Furthermore, a study investigating primary care use for mothers in the BiB cohort found that areas in Bradford that were more deprived had fewer primary care practices, but higher GP consultation rates. Pakistani women in the same study also had higher consultations rates. However, after adjusting for how ill these groups were, they appeared to consult the GP less (Kelly et al. 2016b). As this thesis uses the same study population as Kelly et al. (2016b), it is essential to investigate how levels of deprivation and ethnicity affect children in the BiB cohort.

2.4.2 Secondary data sources for measuring healthcare use

Secondary data comprises data already collected, which is not generated specifically for any particular study. Examples include census data, national population statistics, and, in the case of this research, routine health data. Routine health data is obtained for administrative and clinical purposes without specific a priori research goals, and it has evolved rapidly in recent years in its extent and robustness, as well as being made more accessible to researchers. Consequently, access to routine health data has transformed the research landscape (Benchimol et al. 2015). The key sources of routine health data include the previously discussed disease registers, primary care databases,

health administrative data, HES and hospital medical records. These sources are generated in various health settings and geographic locations, and are cost effective, efficient and have the ability to inform healthcare decisions (Morrato et al. 2007).

2.4.3 Primary care data

Primary care databases are frequently used for epidemiological and medical research and are a valuable source of patient data, as over 98% of the UK population is registered with a GP (Dave and Petersen 2009). Primary care acts as a gatekeeper, with GPs organising referrals to, and receiving feedback from, specialists for different healthcare needs (Vezyridis and Timmons 2016). Almost all GPs use a computerised system, which makes longitudinal databases of patient diagnoses, signs and symptoms, prescribed drugs, and referrals to secondary care a possibility (Gnai and Majeed 2006; Dave and Petersen 2009). It is estimated that around 95% of patient interaction within the whole NHS is with primary care services, contributing to more than 300 million consultations a year. The resultant data is therefore both vast and rich, which enables researchers to create studies that can understand variations in the quality of care between primary care practices (The Kings Fund 2016b). Each primary care database holds slightly different patient information. Some primary care databases have linked hospital episode data, while some do not. Understanding the pros and cons of each database, in terms of their data capture and latency, is a relevant step to help understand whether the approach and results of the research in this thesis can be replicated using other primary care databases. This would allow a comparison of the disease impact and healthcare use of children with CA within other populations in the UK.

Being population based and recorded by GPs in the interest of the patient's health, means the resultant data from primary care databases is derived from a representative sample of the population (Gnai and Majeed 2006). Primary care data is often being used to help identify at-risk patients and drive future clinical research (ResearchOne 2017). These kinds of investigations have revealed

that primary care is under increasing pressure due to the complexity of patient needs. For example, primary care consultations grew more than 15% between 2010/11 and 2014/15, with practitioners making more than 13 million referrals for elective (planned) care in 2014, an annual spend of around £15 billion (McKinsey 2009). These numbers continue to rise, yet services are subjected to yearly falls in funding (The Kings Fund 2016b). The pressures of patient complexity and stretched resources in primary care services have remained largely hidden until recently because of a lack of nationally available data (The Kings Fund 2016b). Both the lack of funding and the lack of analysis of data, which is essential for ensuring primary care services are appropriately resourced to meet the demands of complex and long-term conditions, are concerning. The care of long-term conditions is responsible for 70% of the health service budget (NHS England 2014) and is the main challenge facing healthcare systems, not just in the UK but worldwide (Barnett et al. 2012). Therefore, the demand for more GP practices to share their data for research purposes, and the demand for studies such as the one proposed in this thesis, which analyse healthcare use for patient populations with long-term needs such as CA, are high.

Although there are more than 9,600 primary care practices in the UK, not all contribute their data for research purposes (Vezyridis and Timmons 2016). In the UK there are four longitudinal primary care databases containing electronic primary care records that do contribute their data for research purposes. These research databases are the Clinical Practice Research Database (CPRD 2017), previously known as the General Practice Research Database (GPRD), The Health Improvement Network (THIN 2017), ResearchOne (ResearchOne 2017) and QResearch (QResearch 2012).

The CPRD is a not for profit research database, jointly funded by the National Institute for Health Research and the Medicines and Healthcare Products Regulatory Agency for the DH. CPRD was founded in 1987 and covers approximately 7.1% of the UK population, with larger coverage in London, the South East and the South Coast (CPRD 2017). THIN was established in 2003,

and contains medical records for 11.1 million patients, equivalent to 75.6 million patient years of data, and 562 general practices in the UK. THIN covers 6.2% of the population and has approximately a 50 to 60% overlap with CPRD (UCL 2017). QResearch is a collaboration with the University of Nottingham, and uses data based on 3,400 primary care practices from EMIS health (EMIS 2017). It contains event-level data extended back to 1989 with clinical and demographic data from over 1,243 primary care practices in the UK, a population of over 24 million patients (Kotz et al. 2017).

Participants in the BiB cohort are linked to primary care records from the ResearchOne database, which was developed by The Phoenix Partnership (TPP) in collaboration with the University of Leeds and the UK Government's Technology Strategy Board. ResearchOne has access to 28 million SystmOne (TPP 2016) health records covering Yorkshire and the Humber, East Midlands, the East of England and the North East. SystmOne is a centrally hosted clinical system that enables the sharing of patient records between many provider types. SystmOne is used in 2,700 GP practices in the North of England, resulting in 44 million patients with shareable primary care records. The uniformity of SystmOne in GP practices in the North of England means the data is likely to be of better quality than in other databases (TPP 2016).

2.4.4 Hospital episode statistics (HES)

HES contains details of all patient admissions, outpatient appointments and accident and emergency attendances at NHS hospitals. The use of routine health data for capturing hospital admissions, which includes information on diagnoses, length of stay, operations performed and the characteristics of those patients accessing services (Williams and Wright 1998), helps identify health needs as well as gather information on whether health services are available, accessible, effective and efficient (CDC 2013). HES records cover a wide range of information including patient details such as age, gender, geographic details, when they were treated and what for, clinical information about diagnoses, operations and geographical information such as where the patient lives. The

benefits of HES for this research (and in general) are its ability to monitor trends and patterns in NHS hospital activity. This enables the assessment of effective delivery of care, something which commissioners can base national indicators for clinical quality on. HES data is also longitudinal, which helps reveal trends over time (Health and Social Care Information Centre; HSCIC 2016a). HES data is currently used to identify epidemiology and public health trends to target improving service development. HES also helps to inform government policy, but most importantly monitors the quality of healthcare and seeks to inform patient choice (HSCIC 2011). The clinical diagnostic information of HES data has also been improving over time, in response to concerns around the accurate recording of procedures from consultants (HSCIC 2011).

2.4.5 Medical record review

Medical record reviews are sometimes necessary to capture multidisciplinary outpatient data and referral activity not routinely included in electronic medical records (Vassar and Holzmann 2013). A medical record review is a study using pre-recorded and patient-focused data as the primary source of information, comprising a combination of consultant reports, test results, nursing, allied health professional notes and laboratory tests, often in paper form (Worster and Haines 2004). These may, however, differ depending on the NHS trust, data sharing agreements and continuity of records. Some children also require services out of area (Peterson et al. 2013), which is often not easy to interpret from electronic systems. Medical records that contain consultant letters discussing referrals to specialists and their locations are used to provide the most complete and reliable data source available for understanding the patient care process (Banks 1998). Despite improved access to electronic healthcare records, in order to find detailed information, paper medical records remain a useful source. They also present some challenges, as they contain large amounts of free text information, the nature of which can change dramatically between patients' records. A solution to ensuring extraction is standardised is to decide on the data extraction protocol before beginning data collection (Worster and Haines 2004).

2.5 Statistical approaches

To identify appropriate literature exploring quantitative approaches for analysing healthcare data, the following search strategies were performed. Firstly, when analysing longitudinal data from cohort studies, certain statistical approaches are necessary to help account for confounders in the statistical analysis phase and improve the reliability of the results. Confounding in epidemiological research is a process that can bias results when examining the association between exposure and outcome (Law and Pascoe 2013).

In a previous CA study conducted in Bradford (Sheridan et al. 2013), maternal risk factors for CA were identified. To ensure that these maternal risk factors remain the most significant for children being born with a CA, a step that helps validate the study population of children with CA and is further discussed in Chapter 3, the literature identifying maternal risk factors covered in the previous CA study (Sheridan et al. 2013), and any other risk factors that may be influential, are briefly reviewed. To do this, the Ovid and PubMed databases were searched using the key terms “congenital anomalies” AND “risk factors” with relevant synonyms.

Secondly, as mentioned in Section 2.2.2, in highly diverse populations such as Bradford, there may be more nuanced constructs aside from the child’s CA that makes the child’s needs complex and consequently influences healthcare use. To explore risk factors for healthcare use, the Ovid database was searched using key terms “Comorbidities” AND “Child”, “comorbidities” AND “outcome measure” and “comorbidities” AND “risk adjustment” with relevant synonyms. Searches were filtered to human studies with no date restrictions. Papers were excluded if they referred to multi-morbidities in adults or older people, or were condition specific. Search strategies can be found in Appendix 7. A web-based search was also performed specifically related to directed acyclic graphs and their application in epidemiological studies.

2.5.1 Risk factors for CA

Two UK studies (Bundey and Alam 1993; Sheridan et al. 2013) discuss the role of consanguinity in CA research, one of which was the phase 1 study (Sheridan et al. 2013), which found 2,013 (18%) children were the offspring of first cousins. The offspring of first-cousin unions in phase 1 (Sheridan et al. 2013) were found to be mainly of Pakistani origin, with 1,922 (37%) of 5,127 Pakistani children having parents in first-cousin unions. The most significant risk factor for CA in this study was consanguinity, associated with a doubling of risk for CA (multivariable RR 2.19, 95% confidence interval (CI) 1.67 to 2.85). This risk remained after adjustment for deprivation. Phase 1 (Sheridan et al. 2013) identified CA and explored risk factors in children diagnosed with CA up to age one only. The second UK study (Bundey and Alam 1993) was a five-year prospective study of 4,935 children from different ethnic groups, which found post neonatal mortality and childhood morbidity in children born to consanguineous parents to be three times higher than those from non-consanguineous parents. This study estimates that a possible 60% of mortality in these children could be reduced if consanguinity was prevented.

The Medical Birth Registry of Norway (Stoltenberg et al. 1997) examined all births between 1967 and 1993, and found the risk of CA for children born to non-consanguineous parents was practically equal for all births, independent of ethnicity and level of deprivation (Stoltenberg et al. 1997). In the Pakistani subgroup, however, consanguinity was a major risk factor for CA and the proportion of CA was higher among children whose parents were first cousins or closer (Stoltenberg et al. 1997). Mainly, studies reporting an association between CA and consanguineous parents were conducted in the Middle East (Bromiker et al. 2004; Harlap et al. 2008; Zlotogora et al. 2010; Majeed-Saidan et al. 2014), an area of the world where it is customary to engage in consanguineous relationships. In these populations it is estimated that between 20% and 50% of marriages are contracted between couples who are second cousins or closer (Bittles 2012).

Consanguinity is also apparent in countries where consanguineous relations are not customary, as migrants from countries where consanguinity is common are still highly likely to preserve traditional patterns of marriage, especially if they were from disadvantaged groups, and/or received a lower education in their host country (Harlap et al. 2008). For example, similar to the findings of phase 1 (Sheridan et al. 2013), a German study discovered, when using 20 years of data from 35,391 foetuses, 676 (1.9%) were reported to be the offspring of consanguineous unions. Forty-five per cent of this group were first cousins. The frequency of complex CA was higher in the consanguineous group (3.7%) compared to the non-consanguineous group (1.5%). Consanguineous relationships were found to be the most common among couples of Turkish or Eastern Mediterranean/Maghreb migrants. Ninety-five per cent of all consanguineous foetuses examined in this study were from these backgrounds (Becker et al. 2015).

There is less certainty around other risk factors for CA. In phase 1 (Sheridan et al. 2013), maternal smoking, drinking, BMI, education level, diabetes and age were considered alongside consanguinity, with only maternal age (>34) increasing the risk for white British mothers, and education lowering the risk for all mothers (Sheridan et al. 2013). Maternal smoking is fairly well reported as a risk factor in the literature, yet its relationship with CA remains mixed (Sheridan et al. 2013; Mateja et al. 2012; Patel and Burns 2013; Caspers et al. 2013; Lee and Lupo 2013; Wang et al. 2014; Feng et al. 2014; Honein et al. 2014; Nicoletti et al. 2014; Sullivan et al. 2015; Petersen et al. 2016a; Zwink et al. 2016). Maternal smoking and the risk of cardiac CA is the most frequently reported (Sheridan et al. 2013; Mateja et al. 2012; Patel and Burns 2013; Lee and Lupo 2013, Sullivan et al. 2015), and two studies report no association (Sheridan et al. 2013; Petersen et al. 2016a).

Maternal diabetes, binge drinking, and increased body-mass index (BMI) in combination with maternal smoking were reported to also increase the risk of adverse birth outcomes in three studies (Mateja et al. 2012; Feng et al. 2014; Zwink et al. 2016). A threefold risk of cardiac CA was found among mothers

reporting alcohol use during pregnancy (Patel and Burns 2013), yet five studies reported no association (Makelarski et al. 2013; Sheridan et al. 2013; Caspers et al. 2013; Zhu et al. 2015; Wen et al. 2016). Other risk factors include increased maternal age (>35), (Sheridan et al. 2013; Majeed-Saidan et al. 2014), illicit drug use (Patel and Burns 2013), air pollution (Farhi et al. 2014; Swartz et al. 2015; Girguis et al. 2016; O'Brien et al. 2016), diabetes (Majeed-Saidan et al. 2014) and a potential reduced risk for mothers adopting an organic diet during pregnancy (Brantsaeter et al. 2016).

Studies investigating the impact of drug use during pregnancy also have mixed results (Banhidy et al. 2006; Tata et al. 2008; Lennestal et al. 2009; Brender et al. 2011; van Gelder 2011; Brender 2012; Daniel 2012; Diav-Citrin and Onroy 2012; Koren and Nordeng 2012; Andersen et al. 2013; Vasilakis-Scaramozza 2013; Ban et al. 2014; Lupattelli et al. 2014; Petersen et al. 2016b). However, one anti-depressant drug called Paroxetine was associated with increases in cardiac CA when taken during pregnancy in two studies (Reis and Kallen 2010; Ban et al. 2014), and an anti-epilepsy drug called valproate was also associated with an increased risk of CA (Morrow et al. 2006; Tomson et al. 2007; Tomson et al. 2011; Campbell et al. 2014). The research also points to record linkage to primary care databases as a successful source of data for drug use during pregnancy (de Jonge et al. 2015), with observational cohort studies also endorsed as one of the most important sources for risk characterisation of drugs during pregnancy (Wacker et al. 2015).

2.5.2 Risk factors for healthcare use

When trying to measure healthcare use, there are certain characteristics aside from ill health that may influence the uptake of services. In a study conducted by Kelly et al. (2016b), mothers from the BiB cohort who lived in more deprived areas of Bradford, and women of Pakistani origin, used the GP more. However, after adjusting for how ill the mothers were, those from deprived areas consulted the GP less than mothers who were not living in materially deprived

areas (Kelly et al. 2016b). Furthermore, after controlling for ill health, Pakistani women had lower consultation rates than white British women.

Adjusting for ill health using a measure of multi-morbidity is a recognised method of risk adjustment for evaluations of healthcare use. The severity of illness may not solely be due to multi-morbidity and ill health, it may also be due to other patient characteristics such as socioeconomic status, or the practice to which they belong (Gravelle et al. 2006; Brilleman et al. 2014). When assessing healthcare use to inform the commissioning of healthcare services, risk adjustment represents patient outcomes equally across healthcare providers (Horn et al. 2002; Gorelick et al. 2007; van-Mourik et al. 2015). This allows investigations into the potential external factors influencing the supply and demand of healthcare services, rather than how ill patients are. In the study of healthcare use conducted by Kelly et al. (2016b), a count of unique prescriptions for each mother in the study and a score from a multi-morbidity index called the Charlson Index were used to adjust for ill health (Valderas et al. 2009).

Multi-morbidity refers to the occurrence of multiple conditions in one person, or the co-occurrence of two or more long-term conditions within an individual (Armitage et al. 2009; Diederichs et al. 2011; France et al. 2012; Smith et al. 2013; Lefevre et al. 2014). Multi-morbidity is common in generalist settings such as primary care (Huntley et al. 2012; Booth et al. 2014), where family practitioners act as the first point of contact for patients who may have more than one condition at one time (Huntley et al. 2012). The choice of a multi-morbidity measure is often dependent on the suitability of the measure for the data in question as well as the outcome of interest (Diederichs et al. 2011, Lefevre et al. 2014). There is limited agreement in the literature regarding the number and type of diseases that typify a patient with multi-morbidity (Kenning et al. 2015). This could be due to the nature of what a multi-morbidity outcome measure is trying to do, which is to aggregate a complex reality into single indicators, or due to the difficulties involved in choosing a multi-morbidity measure appropriate to the patient population intended for study. It is important

to adjust for multi-morbidity in order to reveal associations between multi-morbidity, patient socioeconomic status, worse health outcomes, and process measures such as healthcare use, costs and quality of care (Huntley et al. 2012).

The Charlson Index is the most commonly used and robust multi-morbidity measure (Valderas et al. 2009; Huntley et al. 2012; Crooks et al. 2015). Although originally developed for hospitalised patients, it has been adapted and validated in primary care populations (Armitage 2009; Fortin et al. 2010; Huntley et al. 2012; Lu et al. 2013). It has also been found useful for prospectively predicting healthcare costs (Charlson et al. 2008; Charlson et al. 2014). However, it does not capture the variety of conditions relevant for paediatric populations, and it also uses death as the end point for validation. The majority of standardised multi-morbidity outcome measures like the Charlson Index have limited application to paediatric populations, as they are designed for risk adjustment in older people (Horn et al. 2002; Chamberlain et al. 2004; Smith et al. 2013). Two of the most commonly used multi-morbidity measures in paediatric populations are the Paediatric Index of Mortality and the Paediatric Risk of Mortality Score (PRISM) (Horn et al. 2002; Conroy et al. 2015), but they also use mortality as the endpoint for validation, and not all children with complex healthcare needs are expected to die early.

Because of the restricted application of standardised multi-morbidity measures to certain clinical settings and patient populations (da Fonesca 2014), there is a body of literature that attempts to quantify multi-morbidity in other ways. These include counting the number of diseases in each individual (Fishman et al. 2003; Sloan et al. 2003; Groll et al. 2005; Valderas et al. 2009; Brilleman and Salisbury 2013; Booth et al. 2014; Van-Mourik et al. 2015), and also counting distinct medications, which seems reasonable given chronic conditions frequently require repeat prescriptions (Fishman et al. 2003; Sloan et al. 2003; Brilleman and Salisbury 2013; van-Mourik et al. 2015). Simple counts of diseases have been found to be one of the most commonly used measures of multi-morbidity (Valderas et al. 2009; Huntley et al. 2012). Some authors also

suggest simple counts of diseases performed better compared to the Charlson Index when the outcome was to predict healthcare use (Kuhlthau 2005; Brilleman and Salisbury 2013). Counts of the number of drugs prescribed have also been recognised as a relevant measure of severity in primary care populations, especially when combined with diagnosis information (Brilleman and Salisbury 2013).

2.5.3 Confounding

Epidemiological studies typically involve large numbers of variables, which require statistical methods to reduce the dimensionality of the data and reveal underlying associations (Ahrens et al. 2005). Multivariate analysis refers to statistical approaches that have two or more dependent or outcome variables, whereas multivariable analysis refers to statistical models that have multiple independent or response variables (Hidalgo and Goodman 2013). Various multivariate and multivariable techniques are available but the choice of which to use depends on the structure of the data and the aims of the research. It is rarely sufficient to look at the influence of a single variable on the outcome of interest, as most outcomes are the result of the complex interplay of many different exposures. In these situations, techniques are needed that allow the examination of the effect of several variables simultaneously for adjustment, but also for prediction purposes (Ahrens et al. 2005).

Regression analysis using cohort study data allows multivariable investigation of two or more groups of subjects, adjusting for the characteristics that might be acting as confounding factors, and is the method used in this thesis (Hidalgo and Goodman 2013). There is often more than one confounder in a regression model, and it is also possible to include too many confounders, leading to over adjustment. To ensure the inclusion of confounders is appropriate, this thesis uses directed acyclic graphs (DAGs) to determine the minimally sufficient confounding set for all of the three outcomes of interest (Law and Pascoe 2013). DAGs are a fairly new concept in epidemiology, but they are useful for helping to reflect a priori assumptions about cause and effect in a specific

context (Law and Pascoe 2013). DAGs also assist in identifying variables that may be missing from regression analyses, and as such facilitate identifying the minimally sufficient adjustment set for minimising confounding bias (Greenland et al. 1999; Pearl 2000; McNamee 2003; Richiardi et a 2008).

When using DAGs it is important to differentiate between model prediction and model inference. Inference is better suited for scenarios where a conclusion is made based on observable facts. Inference could have been used if the outcome was a variable depicting an amount of healthcare use in a certain time period and the predictors were used to determine the cause of this amount of healthcare use. Given, in this case, that the model's aim is to determine how much healthcare may be used in the future based on a set of variables that may affect the rate of healthcare use, it is logical to use prediction (Bosq and Blanke 2007; Watson 2007). Prediction is primarily concerned with the proportion of explained outcome variation, meaning the greater the R^2, the better the prediction model, thus the model is data specific. Although the model may not be replicable from one dataset to another, the focus is to achieve the largest R^2 using the minimally sufficient set of variables. It is important to minimise the effect of collinearity in prediction models as this can lead to large standard errors, confusing the subset of variables selected, as well as introducing a lack of precision, thus making the interpretation of a model difficult.

As well as identifying confounders, DAGs help us understand the influence of mediators, which if included in a regression model, can yield a statistical bias known as the reversal paradox. This makes the interpretation of an association difficult when estimated with a linear regression, as the inclusion of mediators means controlling for part of the causal pathway. Controlling for part of the causal pathway also makes it difficult to understand the findings of observational studies if a mediator is included, as it adjusts for a proportion of the outcome (Tu et al. 2006). DAGs also have limitations, as they can be an over simplification of the relationships between variables. It is not possible to tell from the DAG if a variable provides a protective or harmful effect (Law and Pascoe 2013). Also, exactly how accurately the variables are collected reduces

the statistical control imposed by identifying confounders using DAGs, therefore, it is important to understand the possibilities for measurement error in the variables used. In study 2, DAGs are used to assist the variable choice for the statistical model.

2.6 Chapter summary

This literature review has explored four main topics. Firstly, a scoping review identified seven key action areas that are fundamental to ensuring a health system is prepared to support children with complex healthcare needs. A logical ordering to these themes was also proposed. Before investing resources into healthcare improvements, there needs to be quantitative evidence that there is reason to do so using longitudinal data analysis. To explore appropriate methods for quantifying children with complex healthcare needs, a study population of children with CA was chosen for this thesis, so the second part of this literature review explored the data collection approaches of CA registers. In doing so, some data collection discrepancies of CA registers were revealed, which might be improved upon using alternative data collection methods. The third part of this literature review explored alternative CA data collection methods. One alternative is to use primary care data to identify children with CA longitudinally – revealing later CA diagnoses and potentially increasing the prevalence of CA. Novel approaches for measuring and quantifying the healthcare use and impact of children with CA on the healthcare service were also discussed. This included linked HES, and detailed information from consultants' diagnoses, which can be found in medical letters within paper medical records. Fourthly, an overview of the current, quantitative approaches to statistically analysing healthcare data was explored. This revealed multiple risk factors for consideration in the statistical analysis, and the use of DAGs and risk adjustment to explore important confounders when regressing healthcare use.

3 Methods

3.1 Chapter overview

As previously introduced, in order to effectively answer the research question, two separate studies with concomitant methods were conducted. Study 1 aims to answer research objective number 2: to estimate the disease impact of children with complex healthcare needs using linked datasets. Study 2 aims to answer research objective number 3: to estimate the healthcare use of children with complex healthcare needs using linked datasets. This chapter explains the methods used for studies 1 and 2 respectively. While both studies share some similarities in that they use the same study population – children with CA in Bradford – each of the studies uses its own specific analytical methods and identifies its own findings. However, the studies are complimentary; they build on each other to present a fuller picture of the complex circumstances of the lives of these children.

This chapter is structured as follows. First, the methodological and theoretical underpinnings that have influenced the selection and development of the methods and approaches used in this thesis are explained. The research methods applied in studies 1 and 2 are largely pragmatic in nature and, as such, draw on research paradigms that were designed to bring about change in the health service. Next, the data sources and study populations used in both studies are explained and described. Finally, the individual analytical methods used in each study are outlined separately.

3.2 Methodology

Beginning a methods chapter with the broad underpinning methodology and theory behind the research question, and then applying a funnelling approach, allows for the presentation of a specific approach to address a manageable

research project (Minichiello et al. 1995). This methodological style takes a concept, in its broadest sense, and converges this into a practical research reality.

3.2.1 Research paradigm

As this thesis explores the healthcare use of children with complex healthcare needs, and seeks to understand the impact that responding to their needs has on the healthcare service, it can be described as health services research. Health services research has no concise definition, but there is general agreement that its purpose is to 'lay the general, scientific foundations for health policy, in order to improve the health of people as much as possible under the constraints of society and nature' (Ahrens et al. 2005: 34). This is an appropriate approach when placed in the context of this research, as complex conditions in children are growing in numbers, attributable to a shift in survival of children with complex conditions and medical advances that have resulted in more effective prevention of deaths (Feudtner et al. 2014). It is essential, therefore, that those responsible for managing healthcare resources recognise this changing scenario and take on a wider, more holistic perspective, one that includes complexity, uncertainty and ambiguity (Hunter 2014).

The health services research in this thesis is approached using quantitative, multiple-methods research. One of the aims of health services research is to answer questions about the efficient delivery of healthcare services, to determine if they are meeting the demands of the population. Health services research proposes an alternative viewpoint to the biomedical approach, which is directed by defining a disease and then treating it. In contrast, health services research adopts a population approach, considering other determinants of healthcare use such as demographics, income, ethnicity and education (Schafer et al. 2011). Health services research is not a methodological discipline, but draws on multiple methodologies to provide unbiased, scientific evidence to help influence health services policy and eventually improve the health of the public (Bowling 2014).

In this thesis, two separate studies are presented, both of which are quantitative, which helps clarify the difference between multiple-methods projects and mixed methods. Multiple-methods projects involve more than one research method, all conducted rigorously and completely, but within one project. The results in all methods are combined, or triangulated, to make a whole (Morse and Niehaus 2009). In this thesis, an accurate reflection of the element of complexity children with CA experience and the variety of contacts they have with the health service are not likely to be well captured by one data source, which is why multiple methods are required. This is because multidisciplinary management requires the integration of care, with the overall aim of improving patient care and their experience of the healthcare service. These aims rely on coordination between primary and secondary care services (Shaw et al. 2011).

Multiple-methods research argues that pragmatism is the most useful philosophy of research for integrating perspectives and approaches (Goodman et al. 2013). Pragmatism is a method of using scientific logic to clarify the meaning, concepts or ideas through investigating their potential relationship with the real world (Nowell 2015). One of the benefits of pragmatism as a research method is its flexibility, as it can serve as a philosophical program for many social and health research studies, regardless of whether that research requires qualitative, quantitative, or mixed-methods approaches. Rather than framing the study of social science research as requiring a commitment to an abstract set of philosophical beliefs, pragmatism concentrates on beliefs that are more directly connected to actions (Morgan 2014).

Pragmatic research is particularly relevant for questions that relate to the health of the population, as these kinds of questions also come with implications for how the created knowledge will translate into practice. Creating knowledge that addresses the complex problems found in healthcare practice is needed. It is these sorts of implications that underpin an integrated knowledge translation

research approach, which is significant for advancing the practice of healthcare professionals (Nowell 2015).

3.2.2 Epidemiological methods

Much of the quantitative research in the field of health services research is completed using epidemiological methods (Schafer et al. 2011), a science that focuses on the occurrence of disease in its broadest sense and aims to understand and control its causes (Rothman and Greenland 2005). In this section of the thesis, the conceptual building blocks of epidemiology and the purpose and scope of epidemiological designs are explained, before moving onto describing in more detail the utility of secondary data in healthcare research. The pivotal role of linking secondary data sources to explain the multidisciplinary care needs of children with complex healthcare needs is also discussed.

The science of epidemiology is distinguished by its focus on groups and populations, rather than individuals. Epidemiology has been described as the distribution and determinants of health-related states or events in specified populations, and the application of this study to control health problems (Last et al. 2001). Health-related states in this context refers to the diseases and causes of death, behaviours (such as the use of tobacco), and the provision and use of healthcare services. Using this definition, epidemiology can be defined using two overlapping perspectives. The first is the biomedical approach, which looks at specific topics such as the aetiology of disease and the prediction of disease trends to facilitate the adaption of the health services to future needs, and the investigation of factors that may affect disease outcomes (Last et al. 2001). The second perspective is the achievement of the aims of the first perspective, by applying them and using them to make improvements to public health. For example, allocating and managing healthcare resources, assessing intervention strategies and evaluating the impact of health services (Ahrens et al. 2011). This thesis draws on both epidemiological perspectives, firstly reporting on the number of children with CA in Bradford and investigating factors that may affect

the disease outcome, and secondly, by measuring their impact on the healthcare service to understand how to better manage healthcare resources.

Epidemiological research also has a pivotal role in healthcare development. At their most basic, epidemiological methods rely on careful observation and use of valid comparison groups to assess whether what was observed, such as the number of cases of disease in a particular area during a particular time period or the frequency of an exposure among persons with disease, differs from what might be expected. Epidemiology also draws on methods from other fields, such as biostatistics and social and behavioural sciences. It is not just a research activity but an integral component of public health, providing a foundation for healthcare action based on science and causal reasoning (CDC 2013).

Research that aims to shape health services delivery and understand the needs of the local population usually remains pragmatic in its methodological approach, motivated by the best means to answer a question rather than being philosophically driven (Broom and Willis 2013). This approach draws similarities with the epidemiological health needs assessment, which provides a framework to help understand the complex healthcare needs of children in the BiB cohort while also establishing priorities for improving local health services (Williams and Wright 1998). The epidemiological health needs assessment guides its users to match the services provided by hospitals and primary care teams to the needs of the population. This can be achieved by combining population-level data with more detailed knowledge of individual patients' needs. In this thesis, the needs of the local population are assessed by capturing prevalence estimates of CA, and individual patient data on healthcare use is examined in unison to help guide recommendations and revise the provision of care.

The epidemiological health needs assessment is also a relevant approach for research that aims to explore the health needs of populations with high levels of ethnic diversity and disadvantaged groups such as the BiB cohort. Proponents of this approach believe that the ability to benefit from care is often worse within

more disadvantaged groups, meaning any estimate of need must take into account socioeconomic status (SES) (Williams and Wright 1998). This is because health and ill health follow a social gradient within societies (Marmot 1999). Many indicators, such as education and poverty, which may predict worse health, can be included in a measure of lower SES. Although confounding or reverse causation are likely to contribute to some SES-health associations, there is also evidence that indicates investments in helping address low SES can improve health in many circumstances (Nandi et al. 2014). The methods adopted in this thesis consider the impact of deprivation and ethnicity, and how this might affect the healthcare use of children with complex healthcare needs.

A final point to note when choosing epidemiological methods to guide research is that finding proof is impossible in this kind of empirical science. This point is especially important in observational epidemiological methods, such as cohort studies. It is not possible to determine whether observed associations are causal, instead they are tentative formulations of a description of nature (Rothman et al. 2008). Although this seems like a counterproductive statement, this tentativeness does not prevent practical applications, but instead keeps us sceptical and critical of our own work and the work of others in the same field (Rothman et al. 2008).

3.2.3 Cohort studies

Cohort studies identify a disease-free population by the exposure or event of interest and then follow participants in time until the disease or outcome of interest occurs. Cohort studies allow the investigator to examine multiple outcomes at once and calculate the rates of disease in exposed and unexposed cases over time, making it possible to calculate prevalence, and relative risks (Song and Chung 2011). It is not possible to infer causality from cohort studies, however, only association can be inferred from the results of an observational study (Sedgwick 2013). Although epidemiology alone can never prove that a

particular exposure caused a particular outcome, it does provide enough evidence to adopt suitable control and prevention measures (CDC 2013). This is a contrast to an experimental study, such as a clinical trial, which uses random allocation to control for confounding (Sedgwick 2013).

The longitudinal nature of cohort studies does, however, enable some assessment of causal hypotheses, as it is known if the exposure of interest occurred prior to the outcome. The measurement of levels of exposure over time, alongside changes in whatever outcome is being measured, also provides insight into dose–response relationships between the exposure and the outcome. It makes it more possible to argue the case for causality when using observational research when higher levels of the exposure can be linked to higher levels of the outcome (Levin 2006).

The main advantages of cohort studies are that they can be used to study more than one outcome, which is useful in complex study populations with many interrelated factors. They can also measure change in exposure and outcome over time, and incidence of an outcome can be measured (Levin 2006). There are also limitations to cohort studies; one of which is the need for a large sample size, which makes them expensive to conduct. They may also require long durations for follow-up, maintaining follow-up may be difficult and there is also the chance for loss to follow up, or withdrawals (Song and Chung 2011). The BiB cohort study (for details refer back to Section 1.4.1), however, was commissioned by the National Institute for Health Research Collaboration for Applied Health Research and Care (Wright et al. 2013), and continues to receive a range of funding from the NIHR, Research Councils and charities, including the Wellcome Trust, to continue to follow up the participants.

3.2.4 Routine health data

The exploratory and novel nature of routine health data for answering questions about healthcare means that the analysis techniques are chosen on a pragmatic basis to fit the data. Here, the strengths of pragmatism in research

are its inclusivity of local and broader socio-political realities, resources and needs (Wisdom and Creswell 2013, Johnson et al. 2007). As mentioned in Section 1.4.2, linking the BiB cohort study to two sources of routine health data, primary care records and HES made it possible for BiB researchers to investigate new opportunities for cost-effective follow-up of health outcomes (Wright et al. 2013). Both governments and research agencies are now recognising and prioritising the use of routine health data for improvements to patient care and, in so doing, transforming health research (De Coster 2006; The Kings Fund 2016b).

3.3 Data sources and data definitions

3.3.1 Data sources overview

Figure 4 describes the data sources used and the variables extracted from each data source for use in the analyses. The data sources were primary care data, HES and referral information to be extracted from paper medical records. The aim of combining these data sources was twofold. First, linking children in the BiB cohort to their primary care data and selecting those children with a diagnosis of CA in their primary care records would create the study population. This study population would therefore consist of children with CA who can also serve as an exemplar for children with complex healthcare needs. Second, the aim was to link HES and referral information to children's primary care records, to understand the contact points children with CA have with healthcare. In order to make a linkage like this possible, a unique identifier is required. This is usually a numeric or alphanumeric string that is associated with a single entity within a given data system. An entity is a data variable that you want to analyse information about. An entity is usually a recognisable concept such as a person or place, or a health event such as a hospital admission (Simplicable 2018).

The single entity used in this research was NHS number. NHS Digital (2018) does not consider the NHS number in itself confidential, it is an administrative

number assigned by the NHS. It is important to mention that the NHS number can be used to identify facts about the individual, which are confidential and sensitive, such as diagnosis details, and care plans. Because of this it must be considered both confidential and sensitive by de-identifying it from the data. To do this, BiB assigns a unique identifier to each individual that can be linked back to NHS number should further information be required from the patient's health record. Unique identifiers make it possible to address the entity of interest, but remove the need for accessing identifiable sensitive health data on each patient. This also makes it possible to join two or more datasets together, a process referred to as deterministic data linkage, or record matching (Crossfield and Clamp 2013; Dusetzine et al. 2014).

Record matching is an important process in data integration and data cleaning. It involves identifying cases where multiple database entities correspond to the same real-world entity. In this context, the purpose is to populate the records of a database with the NHS number for patients or service users where such usage is appropriate. The BiB unique identifier can also link all children in the cohort with their mother's cohort information, which, in this thesis, enabled identification of maternal behaviours that may have influenced their child being born with a CA. This investigation of maternal risk factors is discussed further in study 1. Figure 4 demonstrates the data sources that were linked in this thesis, and the information extracted from each data source in order to quantify the demand of CA on the healthcare service.

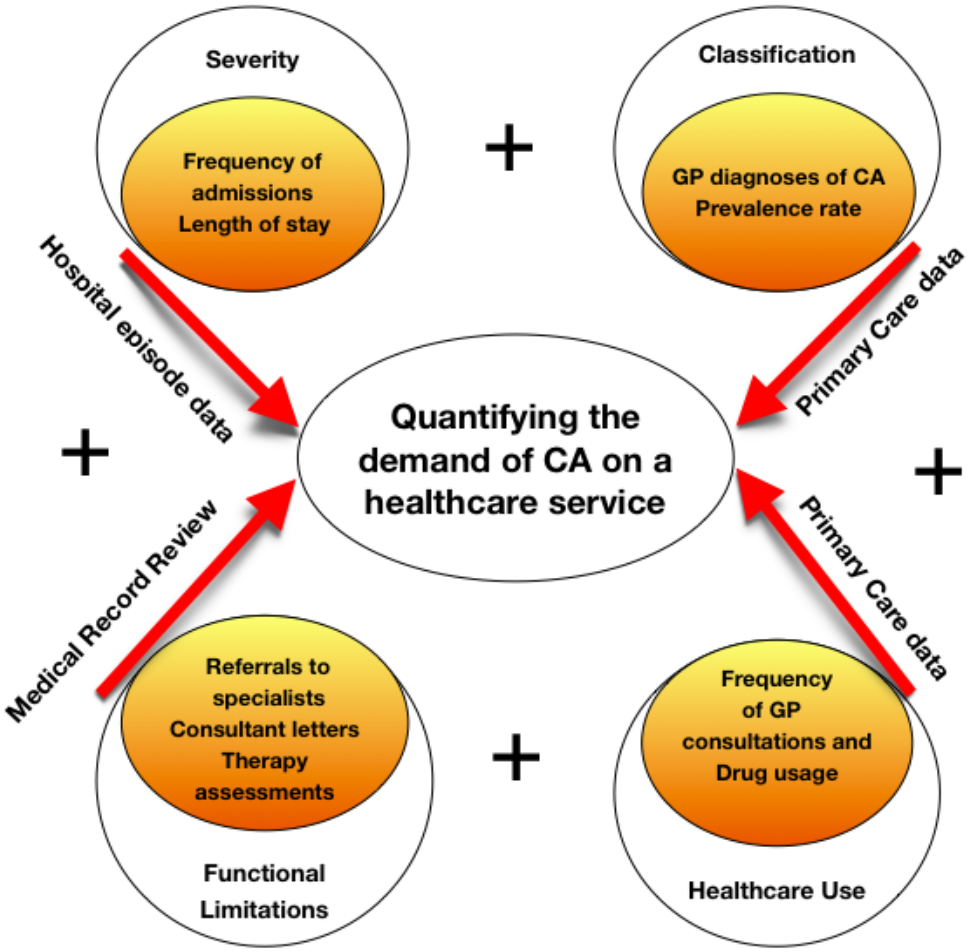


Figure 4: Datasets that were linked and information extracted from each dataset to gather quantitative evidence on the demand of CA on a healthcare service

3.3.2 Local clinical experts

Two of the three clinicians involved in phase 1 (Sheridan et al. 2013), a geneticist and a paediatrician, agreed to act as an advisory role in this study. They provided clinical insight into likely patterns of resource use for children with CA, how referral processes work and the types of admissions to expect for children with CA, as well as describing the methods of phase 1 (Sheridan et al. 2013). The clinicians were consulted at different stages throughout this thesis, and will be referred to in the text as 'local clinical experts'.

3.3.3 Ethics approval

Ethics approval for the original BiB cohort study was provided by Bradford Local Research Ethics Committee (reference 06/Q1202/48). The BiB data application process and research passport approval for access to cohort information and primary care data are available in Appendix 8. A separate ethics application was submitted and approved by BiB for access to hospital medical records (Appendix 9). BiB recruits gave their consent to access electronic primary care records held on SystmOne (TPP 2016). As in the original BiB research protocol, BiB recruits also gave their consent to access HES (Wright et al. 2013).

3.3.4 BiB data

To be eligible for the BiB study, women had to attend the antenatal service in Bradford Royal Infirmary between March 2007 and December 2010, and be booked to give birth in Bradford (Wright et al. 2013). Data is routinely collected using a baseline questionnaire completed by mothers in the Bradford Royal Infirmary Maternity Unit during their recruitment (Wright et al. 2013). All babies born to women who agreed to participate in the cohort study were eligible for recruitment. Figure 5 describes the recruitment figures for the cohort. Since the original data collection outlined in Figure 5, which states there were 13,818 births, additional births have occurred, bringing the total sample size up to 13,857. This is because extra babies were born during the recruitment period to mothers in Bradford Royal Infirmary, but not captured in the antenatal recruitment, or in other words, they were picked up subsequently and retrospectively recruited.

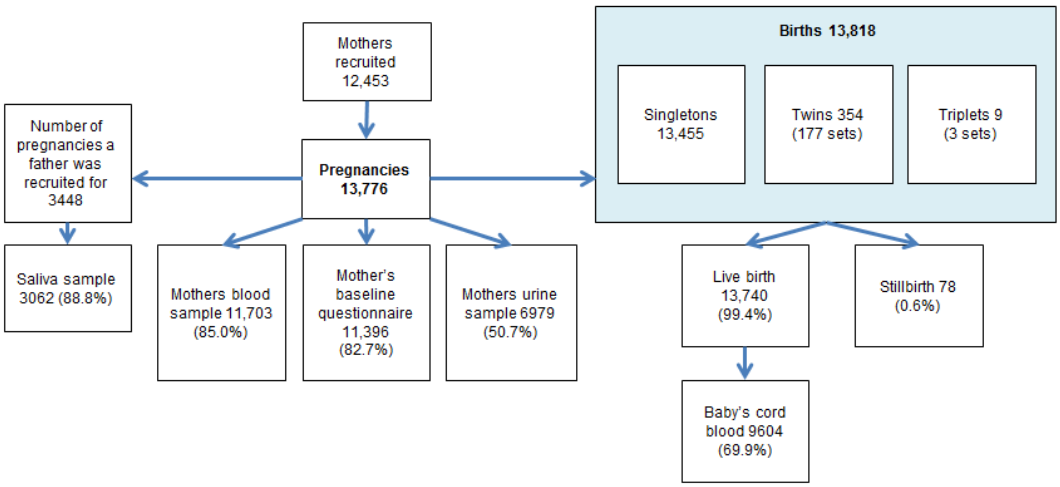


Figure 5: Recruitment statistics for the Born in Bradford cohort (Wright et al. 2012)

3.3.5 Medical records

Some primary care databases contain referral information, which is sent from the GP to other specialists or outpatient services, and some HES data provides information on where the child was referred to after admission. The data sharing agreement between BiB, primary care data and HES did not, however, include referral information. Following discussions with the BiB team, it was also discovered that some services supporting children in Bradford are not captured using the primary care database or HES. In order to understand which services and healthcare activity supporting children in Bradford were not captured by either the primary care database or HES, local clinical experts were consulted. These experts explained the referral process of a newborn baby considered to have complex healthcare needs (outlined in Figure 6), which is not exhaustive, but provides a useful context of the services potentially accessed by a child with complex healthcare needs born in Bradford Royal Infirmary.

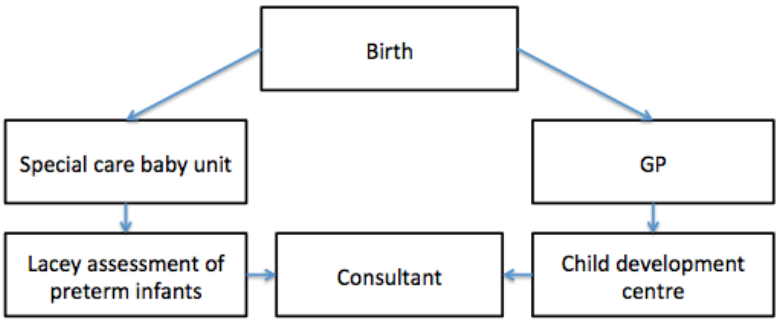


Figure 6: Clinics and service in Bradford coordinating care for children born with complex healthcare needs

The referral process begins with any births linked with a complex condition in hospital being referred to the special care baby unit (SCBU), and assigned a consultant paediatrician. The Lacey Assessment of Preterm Infants (LAPI) clinic screens all complicated births for functional needs from SCBU. The Child Development Centre (CDC) in Bradford, plays a key role in receiving the majority of referrals for children with either diagnoses, or symptoms of a functional need. This is because CDC receives referrals from SCBU, via the LAPI clinic, and therefore children have identified consultants for ongoing/long-term assessment. The CDC receives very few referrals from GPs and these referrals are likely to be for complications that did not present at birth. Once referred to CDC, every child has to be seen within 18 weeks for non-urgent conditions (DH 2013c). Dependent on need, once a child is on the caseload of the CDC they may be referred to a range of different clinics and services, which might include but is not limited to:

- Occupational therapy
- Specialist equipment services
- Orthotics
- Physiotherapy
- Child Psychology
- Cystic fibrosis clinic
- Downs syndrome clinic
- Motor skills clinic
- School nursing team

- Special schools service
- Social services
- Speech and language therapy

All children remain on the caseload of CDC until their goals have been reached, but for most cases, conditions are life long, and these children remain on the CDC caseload until they reach 19 years of age. It is also possible, as advised by local clinical experts, that a child with a complex need is referred to a paediatrician, neonatologist or cardiologist for other conditions that do not meet the referral requirements for CDC. The consultants, whether they work within the CDC or not, record their assessments and diagnoses of each child in letters, which are located in the child's paper medical record. These letters written by consultants, or other specialist professionals, as the result of an outpatient appointment are likely to contain useful, detailed information, which is not available from primary care records. Some primary care databases do have access to letters electronically, but this differs between systems because of variations in data sharing agreements. BiB primary care data did not have access to referral letters and corresponding destinations. Without these letters, ascertainment of accurate healthcare activity using primary care and HES data alone may not represent the healthcare activity of children with complex healthcare needs accurately.

As mentioned in Section 2.4.5, a medical record review is a research method that uses pre-recorded, patient-focused information capturing multidisciplinary outpatient data and referral activity, which may not be routinely electronically collected, to answer a research question (Vassar and Holzmann 2013). In this research, to capture detailed information on services children may receive outside of primary care and hospital services, paper medical records were surveyed. This kind of survey is known as a medical record review.

3.3.6 Study population and rationale for study 1

As introduced in Section 2.3.2, the rate of CA in Bradford was most recently reported by a study that calculated cases of CA up to the child's first birthday, and mirrored the data collection methods used to calculate the national rate of CA (BINOCAR 2014). Understanding the methods used to calculate the prevalence of CA in phase 1 (Sheridan et al. 2013) was an essential step towards informing the collection of CA using primary care data in this thesis, which will henceforth be referred to as phase 2.

In phase 1 (Sheridan et al. 2013), when a child was born with a CA within Bradford Teaching Hospitals Foundation Trust (BTHFT), a standard notification form indicating the CA diagnosis was included in the child's medical record. Phase 1 (Sheridan et al. 2013) followed BINOCAR (2014) guidelines and limited the data collection of CA to age one. Data collection began by identifying all children with a standard notification form in their medical records, indicating the child had a CA diagnosed between the ages of 0 to 1. The recruitment period for phase 1 (Sheridan et al. 2013) was between years 2007 and 2011. These children were then linked to questionnaire data from the BiB cohort. Of 11,396 babies for whom BiB questionnaire data were available, 386 (3%) had a CA. This method did not, however, include any CA diagnosed after the age of one. The rate of CA in phase 1 (Sheridan et al. 2013) was 306 per 10,000 live births, higher than the national average of 227 per 10,000 live births (BINOCAR 2014; Sheridan et al. 2013; CDOP 2016). Risk factors for CA were also explored in phase 1 (Sheridan et al. 2013), of which consanguinity to the first-cousin level was found to be the most significant risk factor (Relative Risks; RR) for CA (RR 2.19, 95% CI 1.67 to 2.85), along with maternal age (>34) for white British mothers (RR 0.42, 95% CI 1.14 to 3.00). Education to degree level or higher was protective for all mothers (RR 0.53, 95% CI 0.38 to 0.75).

Although the phase 1 (Sheridan et al. 2013) data collection method follows official BINOCAR (2014) guidelines, which are in many ways appropriate, BINOCAR (2014) figures report very few CA are registered in the postnatal

period, and only 2% after the age of one. The literature explored in Chapter 2.3, however, raises the question as to whether the 2% estimate of CA cases diagnosed after age one is in fact accurate, or whether this is an underestimation. The reasons for this are twofold. First, because the evidence surrounding the optimal age at diagnosis of CA from official CA registers is unclear, there is speculation regarding whether CA registry figures are underestimated through inconsistencies in the definitions and data variables between different CA registers, and because of the absence of follow-up data. Second, CA research using longitudinal primary care data to find cases of CA diagnosed at ages one year and above, report an increased prevalence. Using age one as a cut-off for CA ascertainment may be leading to under ascertainment of CA and an underestimation or disparity in need and demand for children's healthcare services.

To explore the issue of under ascertainment of CA in Bradford, study 1 uses a phase 2 CA data-collection approach, linking children from the BiB cohort to primary care data to explore and collect CA diagnoses from birth to age five years. Primary care data captures some information well, such as number of prescriptions, number of GP appointments, type of appointment, and diagnoses, but there is also a lack of social and demographic information. As BiB collects and monitors detailed information about demographics, deprivation, clinical outcomes and risk factors, the combined data from primary care and BiB produces a detailed platform for analysis. The objective of study 1, therefore, is to compare the case ascertainment using the phase 2 data collection approach of CA from birth to age five years from primary care linked BiB data, and CA rates reported by national CA registers. If more cases of CA are ascertained using phase 2 than those reported by national CA registers, study 1 will then determine whether magnitudes of association for risk factors reported in a previous study of CA in the same population (Sheridan et al. 2013) persist. New risk factors will require clinical review to ensure their validity. If the risk factors do not appear plausible, it is likely that the data collection method picked up erroneous observations. CA data collection is also compared between CA extracted from the primary care database (phase 2) and those clinically

diagnosed in phase 1 (Sheridan et al. 2013), to determine the accuracy of the primary care diagnoses information.

3.3.7 Study population and rationale for study 2

In order to understand, influence and improve healthcare services for children with CA, accurate measurements of the healthcare services supporting them are required. Longitudinal data analyses for children with CA are needed to capture all aspects of their healthcare use, to both assist with improving health outcomes and reduce inappropriate use of hospitals, achieved by addressing gaps in primary care and focusing on prevention (Marmot 2010; The Kings Fund 2015). Combining various sources of data is a method that helps to identify, manage and coordinate patient pathways for children with CA and multi-morbidities. The results of this kind of analysis have the potential to improve coordination of care and communication among specialists and primary care practitioners in order to develop effective collaborative care models (Luthy et al. 2016). These kinds of measurements are essential to enable those responsible for commissioning and delivering children's healthcare, to make effective decisions about the provision of healthcare services (HQIP 2015).

The literature explored in Section 2.4 highlighted that overall, there is a paucity of research addressing multiple healthcare contact points for children with CA, and those studies that do exist, mainly investigate hospital use for children with cardiac CA (Petersen et al. 2013; Pasquali et al. 2014; Simeone et al. 2014; Simeone et al. 2015; Faraoni et al. 2016; Agarwal et al. 2016; Dawson et al. 2013; Islam et al. 2016), and only two studies were found that addressed the demand on primary care services for children with CA (Billett et al. 2008; Wood and Wilson 2012). To investigate the healthcare use of children with CA from the perspective of both hospital and primary care use, study 2 uses the population of children with CA, between birth and age five years ascertained from study 1, linked to primary care records, HES and referral information recorded in each child's paper medical records. Study 2 investigates the

healthcare use of children with CA, while also addressing the influence of deprivation and ethnicity on healthcare use in Bradford.

3.3.8 Combining studies 1 and 2

Figure 7 demonstrates visually how studies 1 and 2 complement each other using two phases of CA data collection to create a study population for study 2.

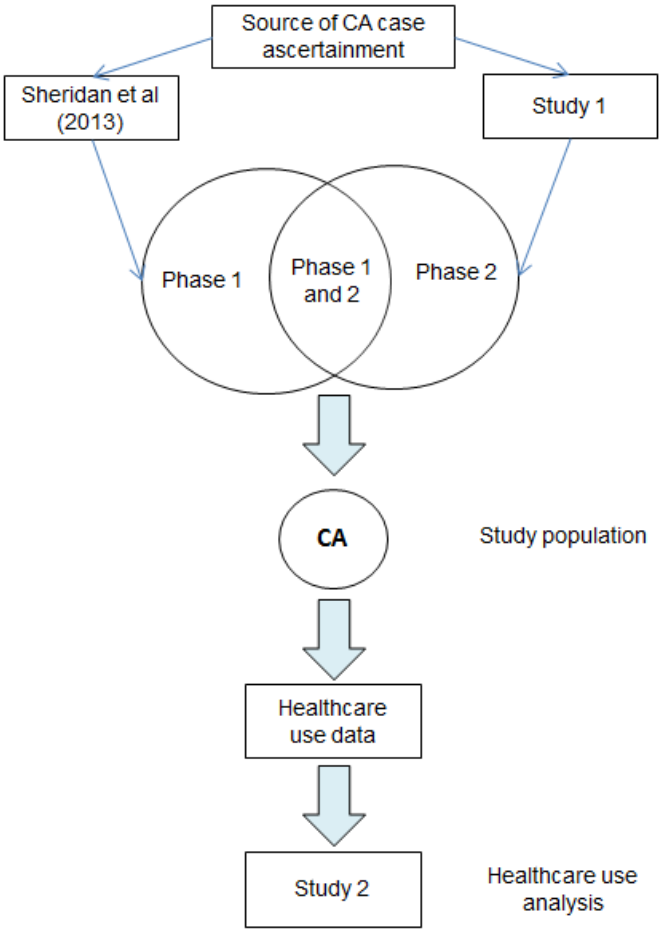


Figure 7: Sources and phases of CA case ascertainment in study 1, providing a study population for study 2

3.4 Analytical methods study 1

3.4.1 Overview

In Section 3.4.2, the iterative process of linking children from the BiB cohort to their primary care data is described. In Sections 3.4.3–3.4.4, the methods for ascertaining cases of CA by extracting medical codes entered by the GP into the primary care system are described. In Section 3.4.5, a validation of clinical coding on phases 1 and 2 is described to determine the agreement between the CA detected in phase 1 (Sheridan et al. 2013), and the CA extracted from the primary care data using the methods from primary care data (phase 2).

Following validation of CA cases, Section 3.4.6 describes how the prevalence of CA was calculated. Prevalence is reported using two different age bands: 0 to 1 years as recommended by national CA registers, and 0 to 5 years due to recommendations from recent scientific literature outlined in Section 2.4.3. Section 3.4.7 outlines the final analysis, which involves investigating maternal risk factors for CA to determine whether magnitudes of association for risk factors reported in a previous study of CA in the same population (Sheridan et al. 2013) persist.

3.4.2 Data linkage

SystmOne, which is the centrally hosted clinical system that enables the sharing of patient records between many provider types (TPP 2016), currently has complete coverage in Bradford. As this coverage has developed over recent years (Figure 8), 11% of children in the BiB cohort were not recorded 60 days after birth. Overall SystmOne coverage is good, with 95% of children's cohort time being recorded as registered at a GP practice (Table 2). Cohort time begins at the date of birth of each child and ends at the date of the primary care data extract, which was July 2016, or at withdrawal from the cohort, or death. Primary care data was linked to each child when there was an exact match for

NHS number, surname, date of birth and gender between SystmOne (TPP 2016) and BiB. Of 13,857 children in the BiB cohort, 97% were linked to primary care data, forming the study population (Figure 9). The scientific data team at BiB provides expertise in the technical aspects of data sharing, developing and maintaining governance structures, and creating and sharing tools for efficient research. Therefore, to ensure the accuracy of the data linkage, the data manager within BiB repeated the linkage process. The average time over which data was recorded in the primary care record was 5.5 years, with a maximum of 7.6 years; in all 74,386 person years of data was available (Table 2). Not all children in the BiB cohort had reached age seven so follow-up was censored to age five.

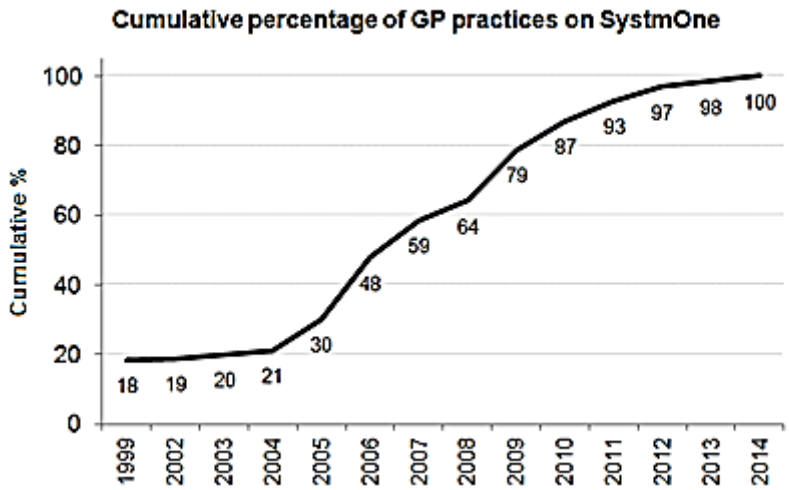


Figure 8: Cumulative percentage of Bradford primary care practices using SystmOne between 1999 and 2014

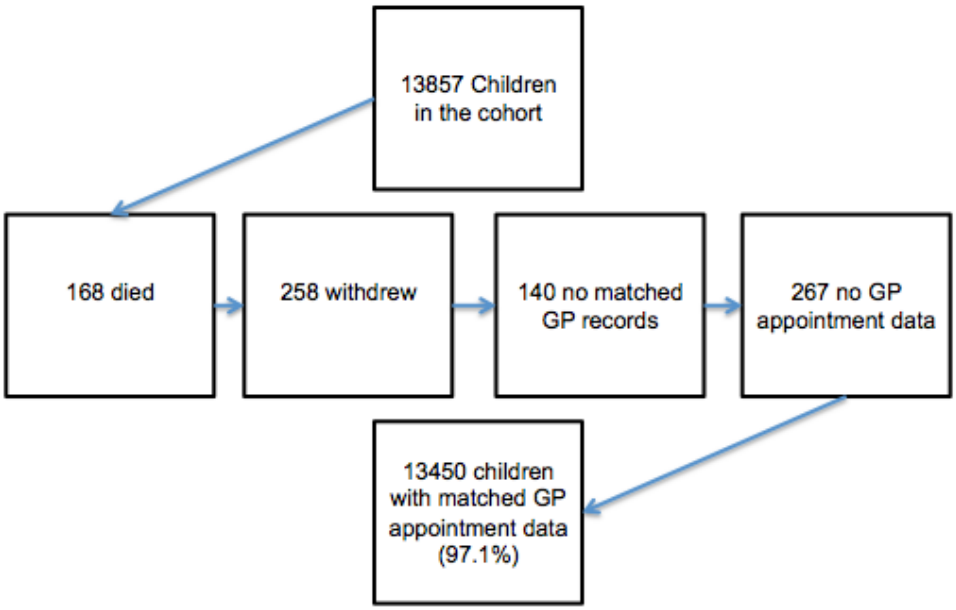


Figure 9: Proportion of the Born in Bradford cohort matched to GP data, and reasons why some participants were not matched

	Mean	Std. Deviation	Median	Min	Max	Person years
Child: cohort time (years)	5.53	1.22	5.56	0.109	7.63	74,386
Child: GP registered time (years)	5.26	1.41	5.33	0.003	7.537	70,690

Child n = 13450

Table 2: Details of the mean time each child has spent in the Born in Bradford cohort and mean time registered with the primary care practice in years

3.4.3 Coding methods and data extraction

There are two different methods of adding codes to diagnoses, one is Clinical Terms 3 (CTV3) and the other is the International Classification of diseases and Related Health Problems 10th Revision (ICD-10; WHO 2010b). Primary care data records patient information in CTV3, and CA classification guidelines are

coded using ICD-10 (WHO 2010b); therefore, to enable extraction of CA diagnoses from primary care data, a codebook was required to convert CTV3 codes to ICD-10 (WHO 2010b). A codebook is a set of condition-specific medical or drug codes used by researchers to search patient medical/clinical and therapy records to identify cases of interest to form study populations (Nicholson et al. 2013). SystmOne (TPP 2016) assigns diagnoses made by the GP in a primary care practice a CTV3 code. CTV3 codes are a standard system for recording patient medical information in UK primary care settings. There is a hierarchical classification system of alphanumeric CTV3 codes, which GPs assign to patient diagnoses, symptoms, referrals made, tests organised or the general process of care, such as patient phone calls or nursing time (Dave and Petersen 2008). EUROCAT (2013) provides the CA coding and classification for all CA registers in Europe, helping to standardise descriptions from clinicians and other health professionals who are responsible for diagnosing CA, creating data that can be analysed for surveillance, and research purposes. The classifications are also organised in terms of conditions that are consistently diagnosed across Europe, and are of reasonable frequency so that yearly prevalence calculations can be meaningful (EUROCAT 2012). This kind of CA classification system does not exist in CTV3.

As not all CA cause long-term, or severe health conditions, EUROCAT (2014) categorises CA into major CA, which are likely to cause significant and long-term disabilities, and excludes a specified list of minor CA and conditions that are poorly specified or related to immaturity at birth (Boyle et al. 2017). The approach in this thesis mirrors that of EUROCAT, including major CA, and excluding minor CA (EUROCAT 2013).

This thesis employed a systematic codebook process, to ensure replication of the data extraction could occur if necessary (Dave and Petersen 2009). The author took the following steps to ensure both the accuracy of CA classification and conversion from CTV3 to ICD-10 codes (WHO 2010b), which was repeated to ensure the same number of CAs were extracted from the primary care database each time:

1. Identifying all diagnoses for major CA as per EUROCAT (2014) guidelines (ICD-10; WHO 2010b) with clinical terms.
2. Repeat step 1 for minor CA.
3. Map diagnoses of CA in CTV3 to diagnoses of CA in ICD-10 (WHO 2010b) using validated cross maps (HSCIC 2016b).
4. As some of the minor CA in the EUROCAT guidelines only have clinical terms, CTV3 codes were matched to clinical terms where possible to prevent missing cases.
5. Microsoft® SQL Server was used to extract CA diagnoses using CTV3 codes from the primary care database and export into Microsoft Excel spreadsheet.
6. Import Excel spreadsheet into Stata and compress duplicate CTV3 codes for the same CA diagnosis for one child entered into SystmOne, retaining only the first diagnosis, using Stata's 'foreach' command.

All CA diagnoses were extracted up to the date the child left the primary care practice (i.e. had died or moved away), the date the practice stopped recording primary care appointment data, or the date of the child's last appointment at time of data extraction (July 2016). A child was classified as having a CA if one or more CTV3 codes for different CA diagnoses were recorded in the child's primary care record at any time during which the child was registered at the practice. Children are likely to visit the GP multiple times throughout childhood for the same health concerns linked to one particular CA diagnosis; therefore, multiple recordings of the same CA diagnosis code entered into SystmOne were compressed into one diagnosis with the earliest date. This step ensured the CA diagnoses recorded for each child were unique, and the number of comorbidities could be counted. The final result was a dataset listing each unique child, their CA diagnoses and the date of diagnosis, the CTV3 code for each diagnosis and the corresponding ICD-10 code (WHO 2010b).

3.4.4 Grouping CA by bodily system

Once all CA diagnosis CTV3 codes were mapped to ICD-10 codes (WHO 2010b), CA were categorised by CA group (the organ system affected), and subtype (the individual disorder) with modification for data on metabolic and chromosomal disorders collected. This mirrors the approach taken by BINOCAR (2014) and EUROCAT (2013), and makes it possible to compare rates of CA by bodily system group, as well as prevalence overall. The modification consists of excluding children with metabolic and chromosomal disorders, which is due to BINOCAR (2014) registering children with metabolic disorders only if they also have a structural CA. BiB includes children with metabolic disorders whether they had a structural anomaly or not. Therefore, to ensure the CA rates from study 1 are as comparable as possible to national CA registers, the most feasible solution was to exclude both metabolic and chromosomal disorders. There are also some further differences in the classification of CA by bodily system group due to an update in the BINOCAR (2014) guidelines. The BINOCAR 2009 guidelines were used to group CA into bodily system groups for phase 1 (Sheridan et al. 2013), whereas the updated 2014 guidelines were used in phase 2, and these have some slight differences in terms of how musculoskeletal (MSK) CA are defined. In the BNIOCAR 2009 guidelines, musculoskeletal (MSK) CA are reported as a standalone subgroup, but according to BINOCAR's updated 2014 (2012 data) guidelines, MSK CA are added to the subgroup of 'other anomalies', which also includes some genetic syndromes and skin disorders. This makes the reporting of CA by bodily system group in phase 1 (Sheridan et al. 2013) and phase 2 CA data collection methods slightly different, the results for which are discussed in Section 4.1.

Further, in the organisation and coding of CA, counts of subgroups are based on cases, not malformations. For example, a child born with several comorbidities, one heart defect, one neurological defect and a limb defect, will count once in 'all anomalies', once in 'heart defects', once in 'neurological defects' and once in 'limb defects'. This also means that the addition of cases in different subgroups does not total the overall count of CA, which can only be

counted from the ‘all anomalies’ categories. A clinical geneticist reviewed the bodily system classifications and ensured the ICD-10 codes (WHO 2010b) given to each CTV3 code were clinically relevant according to the clinical terms.

3.4.5 Validation of clinical coding on phases 1 and 2

It was possible to perform a validation of clinical coding because of the phase 1 (Sheridan et al. 2013) study already identifying CA diagnoses in Bradford. This process helped determine the agreement between the CA detected in phase 1 (Sheridan et al. 2013), and the CA extracted from the primary care data. The CA cases extracted from the primary care data were more likely to be accurate cases, and less likely to be coding errors in the primary care system, if they matched the CA identified by paediatricians in phase 1 (Sheridan et al. 2013). This matching process was made possible because of both phase 1 (Sheridan et al. 2013) and phase 2 data sharing the same unique identifier. If the CA diagnoses matched, this would improve the reliability of any additional CA diagnosed later in childhood (ages 0 to 5 years), and would also help to validate the use of routine health data for CA case ascertainment.

Out of a total 423 children with CA identified in phase 1 (Sheridan et al. 2013), 296 of these children were also identified in phase 2. This means GPs were recording the same CA in SystmOne that were also identified by consultants reporting CA when the baby was born. The validation process was as follows:

1. At least one ICD-10 code (WHO 2010b) between phase 1 (Sheridan et al. 2013) and phase 2 data extracts had to be the same. ‘At least one’, rather than ‘all’, was chosen, as additional diagnoses may have been added since phase 1 (Sheridan et al. 2013) was conducted, so cases would be excluded if the aim had been to match on all diagnoses. Comorbidities and new diagnoses also do not make a difference to the overall prevalence rate calculations.
2. To investigate potential inaccuracy of GP diagnoses coding into SystmOne, full GP records, including every appointment for a sample of

30 children, were reviewed in detail to ensure CTV3 codes were assigned to actual diagnoses rather than referring to appointments related to suspected diagnoses, a validation effort used in other electronic primary care case ascertainment studies (Charlton et al. 2011; Sokal et al. 2013). There was a small amount of free text information in the GP record, which helped determine if the CTV3 code entered was a diagnosis, or, alternatively, investigations of a suspected diagnosis. Using this exercise, all CA that were recorded in the child's record were found to be actual diagnoses rather than investigation.

3. Those children who had a diagnosis of CA that did not exist in phase 1 (Sheridan et al. 2013), but had been recorded after one year, were included as they are likely to have been diagnosed later than the age one year cut-off applied to phase 1 (Sheridan et al. 2013) data collection.
4. Those children with a diagnosis of CA that were completely different between phase 1 (Sheridan et al. 2013) and phase 2 (296 cases), were subjected to a clinical review, to determine if the CTV3 codes were:
    a) referring to the same condition but used different diagnosis codes
    b) were corresponding to different CA diagnoses but these CA diagnoses were medically associated
    c) were referring to CA diagnoses that were non-related.
5. Eighty-three per cent agreement was reached between the 296 cases, when including the cases that matched with the same diagnosis of CA and those that were matched using the clinical review process of 4 a) and 4 b).
6. Those conditions identified in part 4 c) that were totally unrelated, and were also diagnosed before the child was one year old, means they were not picked up by phase 1 (Sheridan et al. 2013), but were recorded by the GP. This could mean that the conditions were not considered important in phase 1 (Sheridan et al. 2013), or were missed, or the GP had coded them incorrectly. Based on the high level of agreement of 83% between phase 1 (Sheridan et al. 2013) and 2, no cases identified in step 4 c) were excluded, as this could be the result of a discrepancy

between data extraction methods and may risk losing children from the sample who have true CA. It will be recognised as a limitation of this study that a small proportion of CTV3 codes are entered into the GP system incorrectly.

As previously mentioned, only 296/423 children with CA from the phase 1 (Sheridan et al. 2013) study were identified in the primary care data, meaning 127 were not. This was because phase 1 (Sheridan et al. 2013) coded some CA diagnosis with ICD-10 codes (WHO 2010b) that were not in the recommended list for inclusion as per EUROCAT (2013) guidelines. This makes it impossible to extract the CA cases coded in phase 1 (Sheridan et al. 2013), when the phase 2 extraction process was driven by a code book following EUROCAT (2013) guidelines. Local clinical experts involved in the coding of CA in phase 1 (Sheridan et al. 2013) were queried about this, and explained that some of the CA they found were so rare that they did not have a diagnosis and a corresponding ICD-10 code (WHO 2010b). This highlights a limitation of the method used in this thesis, that conditions that are not common enough to reach the ICD-10 (WHO 2010b) are likely to be excluded, despite the fact they may still have considerable complex healthcare needs associated with them.

3.4.6 Prevalence calculation

The overall prevalence of CA and the prevalence for bodily system subgroups for children diagnosed ages 0 to 5 years were calculated. Prevalence rates were presented at both ages 0 to 1 and 0 to 5 years, to compare age one rates to national registers BINOCAR (2014), which bases its calculations on 98% of CA diagnoses made up to a child's first birthday. Prevalence was calculated for children ages 0 to 5 years also, to investigate the potential difference in prevalence when including cases diagnosed after age one.

3.4.7 Statistical analysis

The next step of study 1 was to investigate maternal risk factors for CA. Although it may seem outside of the aims of this thesis, investigating maternal risk factors presented another opportunity for validating additional cases identified using primary care data. In phase 1 (Sheridan et al. 2013), maternal risk factors for CA were identified, and the purpose of looking for maternal risk factors in phase 2 was to make sure that the additional CA cases identified are not significantly different from those picked up in phase 1 (Sheridan et al. 2013). If the magnitudes of association are different, this might point to erroneous CA cases and indicate the need for further investigation. To do this, descriptive statistical analysis was first used to identify frequencies and percentages relating to characteristics of the BiB cohort. Only mothers and their children with linked questionnaire data were included in the regression analyses, as the questionnaire data was used to determine confounding factors and create risk factors for the analysis.

The risk factors that were included in phase 1 (Sheridan et al. 2013), already known to be risk factors for CA, were included in the regression analysis, and secondly, with the additional clinical information from primary care records, medication prescriptions data was used to create a variable for anti-depressant drug use during pregnancy, a risk factor deemed to be significant for CA in the literature review. Consanguinity was the most influential risk factor in phase 1 (Sheridan et al. 2013), and remains one of the most strongly linked factors in the literature for having a child with a CA (Bundey and Alam 1993; Stoltenberg et al. 1997; Bromiker et al. 2004; Harlap et al. 2008; Zlotogora et al. 2010; Bittles 2012; Majeed-Saidan et al. 2014; Becker et al. 2015). The other risk factors included were as follows:

- ethnic origin (white British, Pakistani, other); age of mother (<20, 20 to 34, >34 years)
- educational attainment (less than five General Certificate of Secondary Education [GCSE] equivalents; five or more GCSE equivalents at grades

A–C, two Advanced Level equivalents; diploma, degree, or higher degrees; other; unknown; foreign unknown)

- socioeconomic status, measured by a latent variable constructed to capture economic disadvantage from a range of measures collected in the BiB cohort study (Fairley et al. 2013). The measure was dichotomised; address details were used to assign mothers to a Lower Super Output Area (LSOA) and the 2010 Index of Material Deprivation (Index of Multiple Deprivation; IMD (Department for Communities and Local Government 2010)) score was attached. This score was standardised and when mothers moved, the average IMD over the study period was used
- smoking (whether the mother smoked during pregnancy or not); alcohol consumption (drank alcohol during pregnancy or three months before pregnancy [yes or no])
- consanguinity (first cousin, other blood relation [less than first cousin], or non-consanguineous)
- drug use during pregnancy (Any drugs taken in the first trimester of pregnancy or three months before [Yes/No], psychotic drugs taken during pregnancy [Yes/No]).

Drugs were counted as unique prescriptions, not repeat prescriptions, grouped according to the BNF headings. Results for BMI and diabetes (which was tested using an oral glucose tolerance test (OGTT)) were categorised in accordance with WHO guidelines (WHO 2006b; WHO 2006a). These risk factors were estimated using univariate risk ratios (RRs) and 95% CIs for the occurrence of CA with Poisson regression and robust error variance. Risks were calculated for all ethnic groups and separately for white British, Pakistani, and other groups. Variables that were insignificant in the univariate analyses were excluded from multivariable regression models.

To account for multiple testing, which arises due to using seven risk factors repeated for three ethnic groups (28 coefficient estimations), and collinearity, all analyses were repeated with 99.9% CIs to address possible issues of multiple

testing, and reduce chance of type I error. A test for interaction was performed to investigate the association between consanguinity and IMD score and ensure it was not affecting the outcome. This is because there is evidence to show that, in Bradford, consanguineous unions are more likely to be found in deprived neighbourhoods (Sheridan et al. 2013). IMD score was treated as a continuous variable. All statistical analyses were performed in Stata (StataCorp 2013).

3.5 Analytical methods study 2

3.5.1 Overview

The aim of study 1 was to ascertain a study population of children with CA, as an exemplar of children with complex healthcare needs. Study 2 takes this study population and estimates the healthcare use of children with CA. To do this, Section 3.5.2 describes the methods adopted for linking children with CA to their HES and consultant letters, in addition to their previously linked primary care data of study 1. The coding methods for study 2 involved cleaning the data extracted from hospital records and consultant letters, and are described in Section 3.5.3. In the statistical analyses, study 2, aims to investigate what other factors might influence healthcare use for children with CA, aside from their diagnosis of CA alone. The literature investigating such factors was explored previously in Section 2.5. The relationships of factors potentially influencing healthcare use for children with CA are explored in DAGs in Section 3.5.4. Section 3.5.5 explains the statistical model choice, based on the distribution of the data and model residuals.

3.5.2 Data linkage

The process of data linkage to HES data and referral information from medical records is similar to that of study 1, described in Section 3.4.2, and uses the same unique identifier, NHS number. HES data was linked to each child when

there was an exact match for NHS number, surname, date of birth and gender. Of 13,857 children in the BiB cohort, 97% were also matched to HES data. Not every child had a hospital admission, however, and the number of children with at least one (non-birth) hospital event was 5,223 (38%). The number of admissions ranged from 0 to 66 per child. Hospital events included admissions for elective procedures, other emergencies, and A&E presentations. The average time over which data was recorded was the same as the time span for primary care data, which was 5.5 years, with a maximum of 7.6 years, giving 74,386 person years of data. To ensure the same time span for analysis as the primary care linked BiB data, HES data was also censored for children aged 0 to 5 years. Consultant letters containing referral information, which were contained in the paper medical records for each child, were linked to the primary care and hospital care dataset using the same unique identifier.

3.5.3 Coding methods and data extraction

3.5.3.1 Primary care data

The same dataset of BiB children with CA diagnosed between ages 0 to 5 years, linked to their primary care records, was used in study 2, but additional variables were extracted for this analysis. Drug prescriptions for each child were extracted, in order to understand how many unique prescriptions were provided. This information was used to enable risk adjustment for ill health in the regression model, a process that was described in Section 2.5.2 of the literature review, and in this analysis allows other factors that may be influencing healthcare use, aside from ill health, to be investigated. Additionally, primary care data was used to extract the number of consultations children with CA had with their GP, in order to understand the service impact of children with CA. The average number of primary care consultations per year and over the five-year period, for children with and without CA, stratified by ethnicity, is described.

3.5.3.2 Hospital episode statistics

HES data, unlike primary care data, codes diagnoses in ICD-10 codes (WHO 2010b). However, it was not the purpose of linking to HES data to retrieve CA diagnoses. The purpose was to link HES data to children with an identified CA, to investigate the use of hospital services for each child, mirroring the age for CA case ascertainment of 0 to 5 years old. The HES data was organised by the author into different types of hospital events, which included admissions for elective procedures, other emergencies, and A&E presentations, therefore HES data can be thought of as the use of hospital services, rather than simply admissions, as this terminology infers an emergency admission only. The average number of hospital admissions per year and over the five-year period, for children with and without CA, stratified by ethnicity was described. It was also possible to identify the most common cause for children using hospital services, both with without CA.

3.5.3.3 Medical record review

In order to gain access to consultant letters containing detailed referral information, paediatric medical records were requested. The paper medical records for a sample of 200 children with and 200 without CA were reviewed. The 200 cases with CA were selected at random from the study population established in study 1. This was a practical, convenience sample as the subjects were selected because of their accessibility and proximity to the researcher. The sample had to include children with CA, and when dealing with rare diseases, convenience samples are often the way forward in order to create a study population that contains the exposure of interest (Vassar and Holzmann 2013). Although larger sample sizes reduce the chance of sampling error, medical records are known to contain high frequencies of complex information, which is often interchangeable between records (Vassar and Holzmann 2013). A small sample size was therefore chosen, based on the exploratory nature of the medical record review and the feasibility of performing this by hand within the time scale of this study.

The BiB scientific team, who had previously performed medical records reviews, advised 20 minutes per medical file is to be expected in order to extract the relevant information. To cover 400 medical files, a period of one month was estimated, which equates to reviewing three medical records per hour, and 18 per day. To make sense of the information in medical records, data extraction forms are required to ensure the data was abstracted reliably (Worster and Haines 2004). Well-designed data abstraction forms limit the possibility for misclassification during abstraction, and ensure unambiguous variable definitions (Banks 1998; Worster and Haines 2004). A standardised data extraction form was designed, and reviewed by a clinician to ensure it was structured to reflect the flow of data recorded in patient notes. The data extraction form was also piloted to accumulate the number and type of referrals to different multidisciplinary services (Appendix 10). Medical records were not removed from the hospital medical records library for data protection reasons, therefore all data extraction was completed on the hospital grounds by the author. Data points in the extraction forms that were missing in at least 10% of the sample were dropped, in order to avoid systematic differences between subjects (Simon et al. 2014).

3.5.4 Directed Acyclic Graphs

In study 1, there was a considerable body of research highlighting the most likely risk factors for CA, which had also been further validated in a statistical model in phase 1 (Sheridan et al. 2013). For study 2, there was some literature identified in Section 2.5.3, which highlighted potential risk factors for healthcare use, but limited previous analyses of this kind have been performed before with multiple sources of routine health data. Some of these potential risk factors included diversity and deprivation (The Kings Fund 2016b), variations in GP practice provision, ethnicity and ill health (Kelly et al. 2016b). As the literature supporting risk factors for healthcare use was not as extensive as the literature supporting risk factors for CA, DAGs were a valuable tool in study 2 to explore suspected relationships between risk factors. Risk factors that may influence

healthcare use, as well as identifying mediators for the statistical analysis phase, were explored using DAGs.

The open access browser tool DAGitty (Textor 2011) was used to construct a DAG using each of the three types of healthcare use as the outcome and CA as the exposure, and the results were exported as images presented in Figure 10, Figure 11 and Figure 12. The three outcomes were the use of hospital services, primary care consultations and referrals to multidisciplinary specialists. All DAGs demonstrate the minimally sufficient set of confounding factors suggested by the DAG for adjustment in the statistical analyses. DAGitty highlights confounding variables in red and causal pathways in green. Variables depicted in blue are ancestors of the outcome but are not confounders.

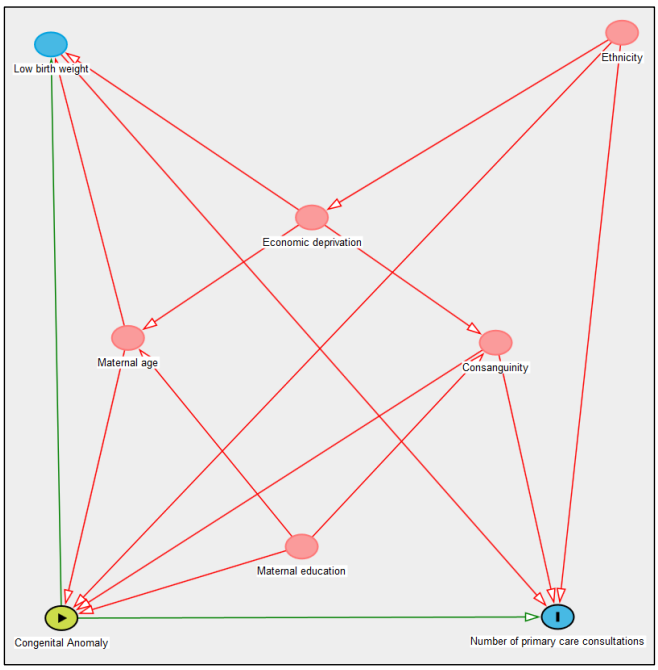


Figure 10: Assessing confounding on the relationship between primary care consultations and children with CA

Minimally sufficient set: Consanguinity, Economic deprivation, Maternal Age, Maternal Education, ethnicity.
Mediator: Low birth weight

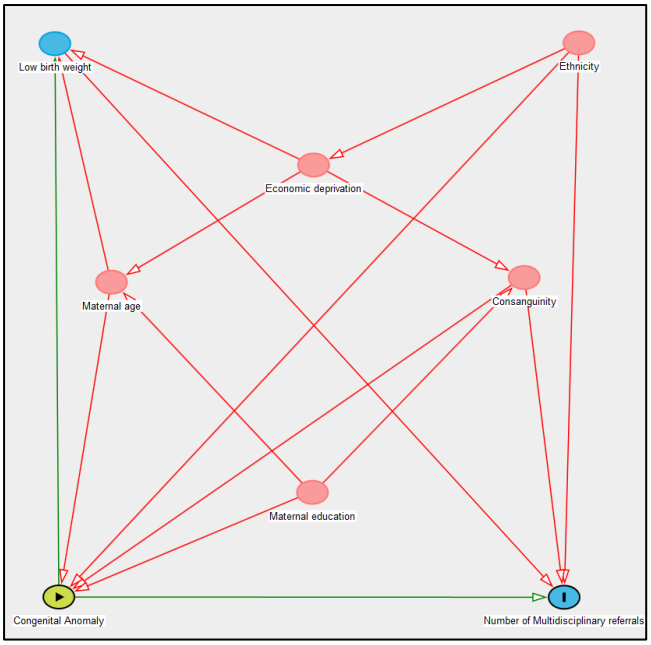


Figure 11: Assessing confounding on the relationship between multidisciplinary referrals to specialists, and children with CA

Minimally sufficient set: Consanguinity, Economic deprivation, Ethnicity, Maternal Age, Maternal education

Mediators: Low birth weight, Number of GP appointments, use of hospital services

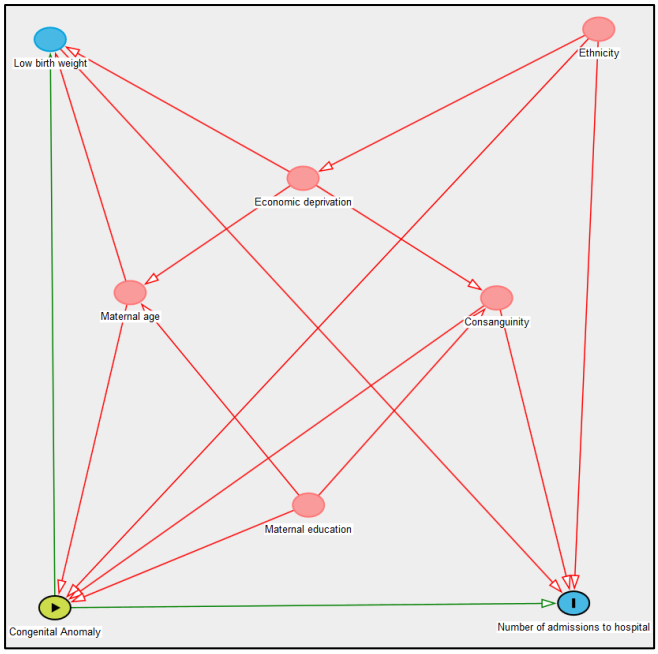


Figure 12: Assessing confounding on the relationship between the use of hospital services and children with CA

Minimally sufficient set: Consanguinity, economic deprivation, ethnicity, maternal age, maternal education

Mediator: low birth weight

The DAGs suggest for all three healthcare use outcomes that the confounders were:

- maternal age (<20, 20 to 34, >34 years)
- educational attainment (low education (<5 GCSE equivalents or other education), high education (5>GCSE equivalents at grades A–C or two Advanced level certificates or diploma, degree or higher degree (Department for Education 2014c)))
- economic deprivation (economically deprived, not economically deprived (measured using a means-tested benefit status. In the UK, being in receipt of means-tested benefits is recognised as a measure of income poverty, as these benefits are frequently the only source of income and are paid at rates that put individuals below standard poverty lines (Platt 2007)))

- ethnicity (white British, Pakistani, Other) and consanguinity (non-consanguineous, first cousin, second cousin, other blood (any relation)).

All covariates were entered into the model as a categorical variable to allow for possible non-linearity in the relationship between the multi-morbidity measure and relevant outcome. Low birth weight was identified as a mediator in all DAGs, as it lies between the exposure and the outcome, thus it will not be included as a confounder.

3.5.5 Statistical analyses

3.5.5.1 Outcomes

The three outcomes were primary care consultations, the use of hospital services, and referrals to specialists. The BiB questionnaire data contained the data for the variables likely to be confounding the relationship between healthcare use and CA; therefore, only children with linked questionnaire data were used in the analyses. Healthcare use in the BiB cohort was summarised using standard descriptive statistics. Both primary care consultations and the use of hospital services were counted as one per day, even if multiple appointments in the same day were recorded, as many of the appointments occurring on the same day were episodes that ran over time, or were duplicates. A count of the number of primary care consultations and use of hospital services equates to the number of healthcare visits over the year, which is expressed as a rate. Primary care consultations and use of hospital services were expressed per year of observed primary care registered time, which takes into account any periods the child may not have been registered with the primary care practice, withdrawals from the cohort, or deaths. Counts of referrals to specialists were made for children with and children without CA on a continuous scale.

3.5.5.2 Regression analyses

Negative binomial regression was used to model primary consultations and use of hospital services. Negative binomial regression models adjust for over-dispersed count data, and have one more parameter than a Poisson model, meaning they can adjust for the variance independently of the mean. The data distribution of primary care consultations and use of hospital services were examined using histograms (Figure 13 and Figure 14), which confirmed a positive skew in the primary care consultations and use of hospital services. The conditional variance also exceeds the conditional mean (Figure 13: mean = 29.2, variance = 367.7; Figure 14: mean = 0.67, variance 3.35), which is a common characteristic of over-dispersed count data (Hilbe 2011). Count models require a mechanism to deal with observations made over different time periods. These differences in observation periods are adjusted for by including the log of the exposure variable in the model with the coefficient constrained to 1, and are superior for analysing rates as a response variable because they make use of the correct probability distributions. The exposure variable indicates the number of times the event could have happened. As count models are estimated using maximum likelihood, and the behaviours of maximum likelihood estimators in small samples are largely unknown, negative binominal regression should only be used with samples sizes larger than 100, which was not a cause for concern in this sample of 13,857 children.

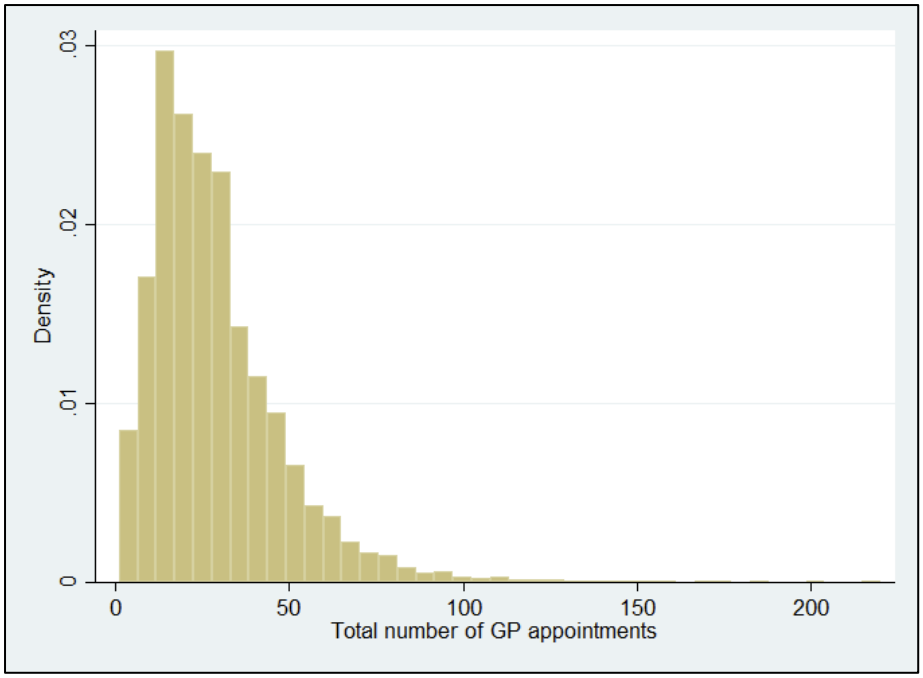


Figure 13: Distribution of the number of primary care consultations in the Born in Bradford cohort

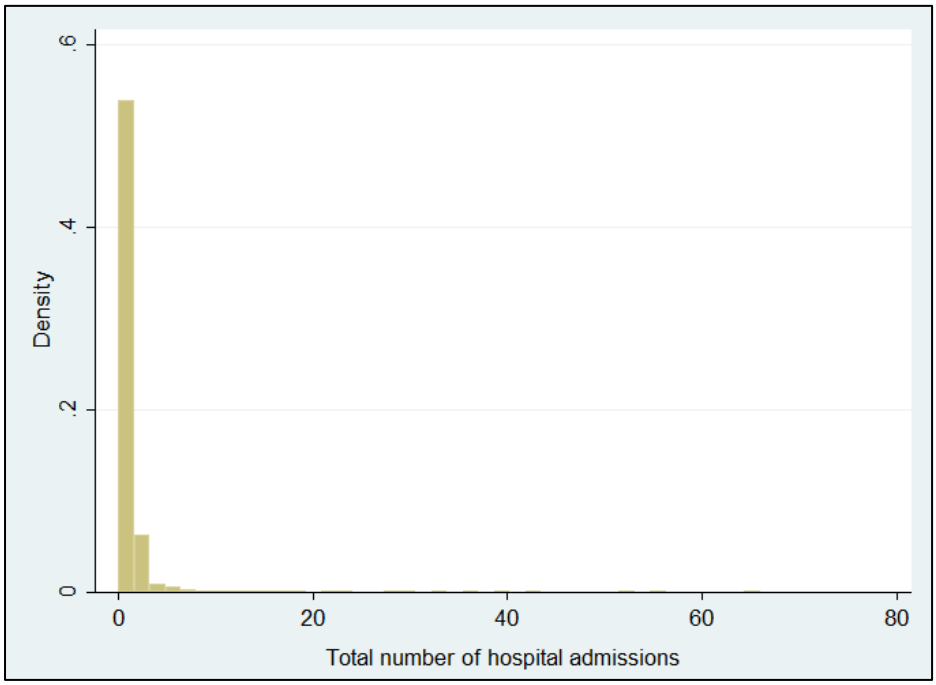


Figure 14: Distribution of the number of hospital admissions for children in the Born in Bradford cohort

For the analysis of referrals to multidisciplinary specialists, however, the sample size was much smaller, meaning negative binomial regression was not

appropriate. Instead, a linear regression was performed on the number of referrals to specialists for children with and without CA.

3.5.5.3 Adjusting for confounders and ill health

Three separate models were used to estimate healthcare use for each separate outcome. The exposure for all three models was all children in the BiB cohort, with and without CA. This is because the measurement of healthcare use, should not only focus on current health, but also factors which influence future health and could further be modified by healthcare services (Forrest et al. 2004). Constructing the model in this way helped determine whether CA was indeed the variable driving the most healthcare use, or if other confounding factors, such as deprivation discussed in Section 3.5.4, were the bigger drivers. Firstly, model 1 estimates univariate analyses, thought of as what is actually observed. Model 2 adds other covariates that were determined to be confounding factors in Section 3.5.4. Model 3 adjusts for confounders established in model 2, and also adds measures of underlying ill health, a risk adjustment method discussed in the literature review (Section 2.5.2). As mentioned in Section 2.5.2, controlling for ill health was necessary to understand whether a child's CA is the primary factor influencing healthcare use, and to explore if, after controlling for ill health, other socio-demographic factors such as deprivation and ethnicity affect healthcare use.

To adjust for underlying ill health, a count of unique prescriptions per child, previously touched on in Section 3.5.3.1, which were recorded in the primary care data, and a count of the number of CA comorbidities per child established in study 1 were used. Incidence rate ratios (IRR) are reported to compare the rate of primary care consultations and use of hospital services for children in the BiB cohort overall, and for children with and without CA. For referrals to specialists, coefficients are reported and a mean value is reported for children with and without CA, with a standard error. Average marginal effects were calculated for all models to aid the practical interpretation of effect sizes (Williams 2012).

Because there are multiple outcomes and multiple models, Figure 15 helps clarify how each model is constructed.

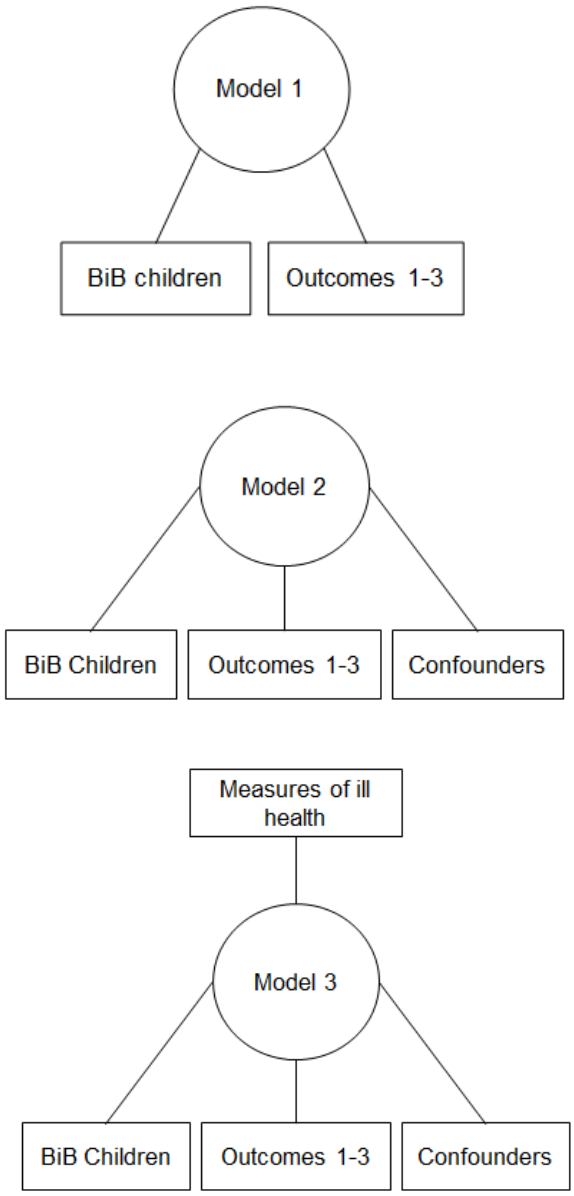


Figure 15: Variable inputs for models 1 to 3 used to model healthcare use for children with CA

Study 2 also stratifies the statistical analysis by children with CA, to investigate differences in healthcare use for children with and without CA when considering certain confounding factors. This regression was adjusted for the same

confounders determined to influence healthcare use identified in Section 3.5.4, and reports relative risks of having increased healthcare use due to confounding factors.

3.5.5.4 Interactions and model fit

To assess the relationship between CA and the level of deprivation, a test for interaction was performed between whether the child had a CA and the level of deprivation for primary care consultations and use of hospital services. This is because in phase 1 (Sheridan et al. 2013), children in deprived neighbourhoods were more likely to be from consanguineous unions, which was the most significant risk factor for CA (Sheridan et al. 2013). As new variables and a different regression approach are introduced in study 2, to ensure the models were not over fitted, model fit statistics were checked for each model. These were the adjusted R-squared for the linear regression used to model multidisciplinary referrals, and, as there is no equivalent of an R- squared statistic in the negative binomial regression output, the likelihood ratio test was used. Residuals were also checked for the disturbance term in each model to determine if there were any significant elements of unexplained variation in the fitted model. Figure 16 and Figure 17 display the residual plots for model 2, adjusted for confounders, using primary care consultations as the outcome. The residuals were similar for each model and each outcome so the rest of the plots were not included. The residuals are approximately normal with a slight skew. The skew is not a concern, however, as in sample sizes over 200, normality is not an imperative assumption as the central limit theorem ensures the distribution of the disturbance term will approximate normality (Rothman et al. 2008). All statistical analyses were performed in Stata (StataCorp 2013).

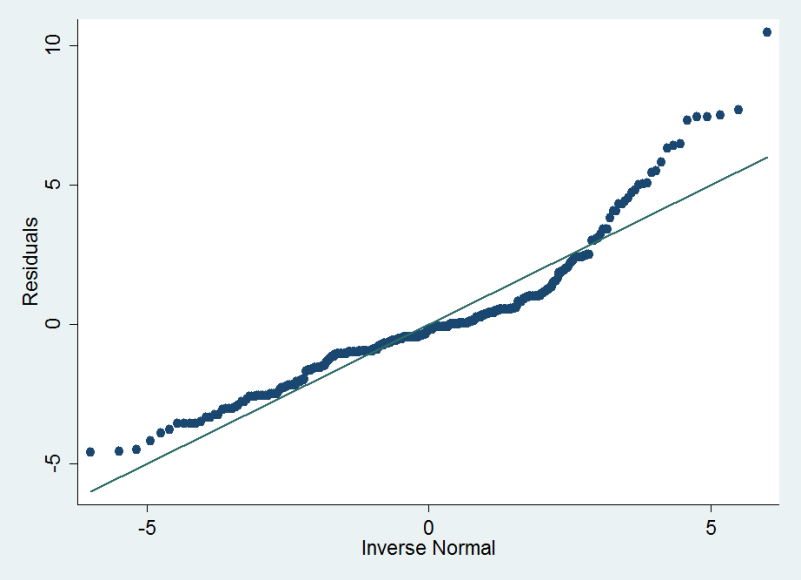


Figure 16: Plot of the model residuals for model 2 with primary care consultations as the outcome against the normal distribution

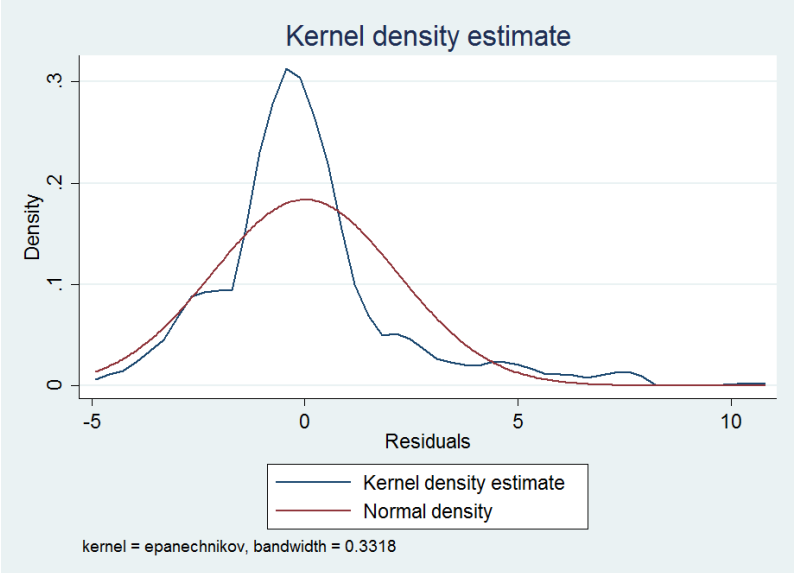


Figure 17: Kernel density estimate to check normality of model residuals for model 2 with primary care consultations as the outcome

4 Results

The results for studies 1 and 2 will now be described. Section 4.1 describes the results for study 1, which compares the number of children with CA extracted from BiB data using phase 1 (Sheridan et al. 2013) and phase 2 methodologies combined, with numbers in national CA registers. Study 1 also presents the results of regression analyses exploring maternal risk factors for CA. Section 4.2 describes the results for study 2, which uses descriptive statistics and regression analyses to describe the healthcare use for children with CA. Healthcare use includes primary care consultations, the use of hospital services and referrals to specialists. Confounding factors that influence healthcare use aside from the child's CA and consequential ill health are also presented.

4.1 Results for study 1

4.1.1 Results of the validation of clinical coding on phases 1 and 2

In Section 3.4.5, the methods for validating clinical coding between phase 1 (Sheridan et al. 2013) and phase 2 were described to determine the agreement between the clinical coding of CA in phase 1 (Sheridan et al. 2013) and the clinical coding used to ascertain CA in phase 2 (Section 3.4). As well as the 296 children that were matched between both phases 1 and 2, a further 127 children with CA were not matched (Figure 18). Considering the characteristics of the 127 children more closely, their average time registered with the GP was 5.2 years, and the average number of GP appointments was 35. This means that not visiting the GP could be ruled out as a reason for missing CA diagnoses from the primary care data. The primary care records did indicate, however, that four children (3%) died before they registered with the GP, 29 children (23%) had changed GP practice once, eight children (6%) had changed GP practice twice, and a further four children (3%) had changed GP practice three times (data not shown). Changing GP practice can result in a loss

of data and may mean CA diagnoses did not reach the primary care system. Some children (23/18%) had CA diagnoses recorded in phase 1 (Sheridan et al. 2013) that was outside of the recommended CA chapter of the ICD-10 (WHO 2010b). The diagnoses for these children were reviewed by local clinical experts to determine why they were included in phase 1 (Sheridan et al. 2013) if they were not a CA according to guidance from national and international CA registers (BINOCAR 2012; EUROCAT 2013).

These 23 children (18%) had ICD-10 codes (WHO 2010b) related to conditions that may be rare, or genetic, or classed as a CA by a paediatrician, but had no equivalent ICD-10 code (WHO 2010b) in the CA chapter of the ICD-10 (WHO 2010b), so they were assigned an appropriate alternative. Conditions that were found to fall outside of the CA chapter of the ICD-10 (WHO 2010b) are listed in Appendix 11. Further inspection of the clinical terms for the 23 children with ICD-10 codes (WHO 2010b) outside of the CA chapter revealed that some of the diagnoses did have an equivalent CA ICD-10 code (WHO 2010b), and were coded incorrectly in phase 1 (Sheridan et al. 2013), but some could not be allocated an ICD-10 code (WHO 2010b) even though local paediatricians were certain of the diagnoses being CA.

4.1.2 CA case ascertainment

Using the methods for study 1 described in Section 3.4, an additional 437 children with a CA were identified using primary care data as a source of CA case ascertainment (Figure 18). These included children aged 0 to 5 years compared to children aged 0 to 1 year, using the methods described in phase 1 (Sheridan et al. 2013). In order to compare the rates of CA using phase 1 (Sheridan et al. 2013) and phase 2 methodologies with the rates of CA reported from the national CA register (BINOCAR 2012), a total of 1,408 CA were discovered in 860 children after the exclusion of minor CA. This means that although 860 individual children were identified, some of them had more than one CA.

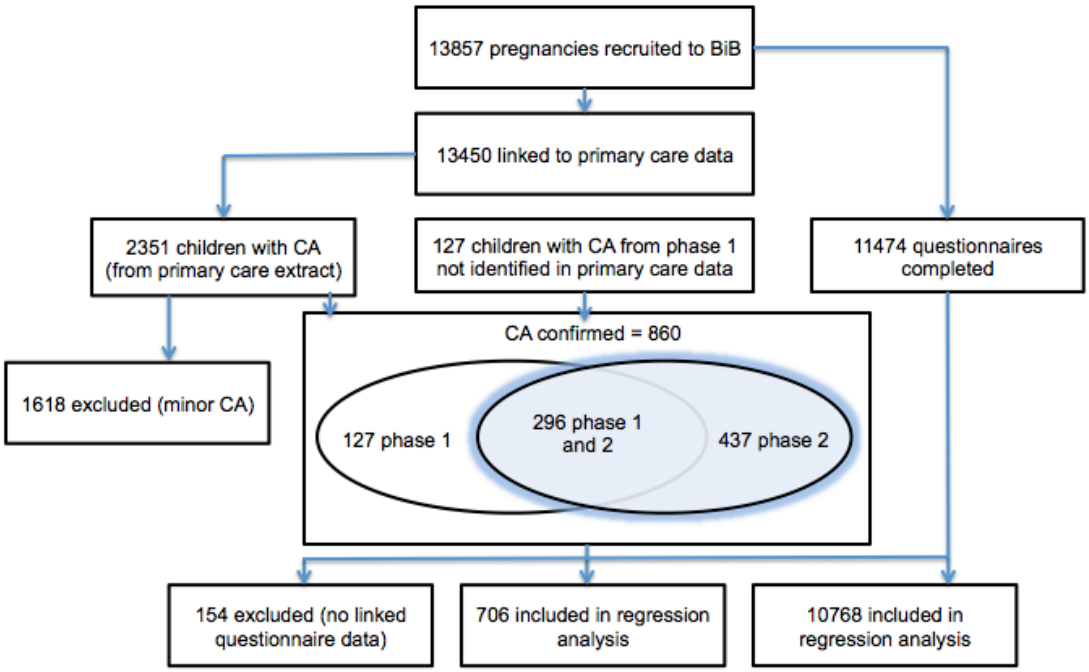


Figure 18: Flow diagram of steps taken in study 1 to identify CA using primary care data, and those CA cases identified in phase 1, phase 1 and 2, and phase 2 respectively

Table 3 compares prevalence of CA discovered in phase 1 (Sheridan et al. 2013) with national data reported by BINOCAR (2014), and the prevalence of CA reported in phase 2 with national rates. Table 3 demonstrates that in 2014, BINOCAR reported the prevalence (based on 2012 data) for CA, excluding chromosomal disorders, at 184 per 10,000 live births (Table 3).

All live births in the BiB cohort (n=13,857)					BINOCAR			
	Total CA*		Total ex Metabolic and chromosomal disorders*		Total	Live births only (259,714)	Live births and stillbirths (260,927)	Total excluding chromosomal anomalies
Age (years)	0<1	0<5	0<1	0<5				
Any CA	432.9 (399.2, 468.9)	620.6 (580, 663.4)	376.0 (344.5, 409.8)	571.6 (532.3, 612.8)	226·5 (220.8, 232.4	168·2 (163.2, 173.3)	171·5 (166.5, 176.6)	183·6 (178.4, 188.8)
Nervous System	93.8	215.1	73.6	192.7	26·4	10·2	10·9	23·6
Heart	91.7	122.7	90·9	116·2	60·2	50·7	51·8	51·4
Respiratory	11·5	16.6	10·1	14·4	9·8	6·3	6·6	8·9
Oro-facial clefts	25.3	27.4	25.3	25·9	14·3	12·6	12·9	13·2
Digestive system	39.7	48.4	35.4	37.5	18·1	15·3	15·7	16·2
Abdominal wall defects	2·2	2·9	2·2	2·9	9·1	5·3	5·4	7·3
Urinary	49.1	64.2	44.0	49·8	27·8	22·1	22·5	26·7
Genital	37.5	51.2	37.5	44.7	17·9	16·9	17·1	17·4
Limb	44.7	57.7	44·0	53·4	34·9	28·9	29·6	32·2
Other / syndromes					6·5	4·7	4·8	6·06
Skeletal dysplasia	5·8	18.0	5.1	12·3	1·5	1·0	1·0	1·5
Genetic syndromes	13.0	17.3	11·5	14·4	4·9	4·0	4·0	4·6
Sequences	7·9	10·8	7·9	10.1	2·3	1·3	1·4	-
Chromosomal	25·3	32·5	0·00	0·00	43·0	14·9	16·6	-

Table 3: Comparison of CA prevalence rates per 10,000 live births between those found in phase 1 and those reported by BINOCAR. Rates of CA found in phase 1 are reported for ages 0 to 1 and 0 to 5 years. *Total CA including metabolic and chromosomal disorders, comparing case ascertainment between CA diagnosed 0 to 1 and 0 to 5 years old.

If only CA ascertained in the primary care data until the child's first birthday is included, study 1 reports the CA rate at 376 per 10,000 live births, also excluding metabolic and chromosomal disorders. Including all cases of CA ascertained in the primary care data until the child's fifth birthday, study 1 reports the CA rate at 571.6 per 10,000 live births, excluding metabolic and chromosomal disorders. The reasons for the exclusion of children with metabolic and chromosomal disorders, as mentioned in Section 3.4.4, is because BINOCAR (2014) registers children with metabolic disorders only if they also have a structural CA. BiB includes children with metabolic disorders whether they had a structural anomaly or not. Therefore, to ensure the CA rates from study 1 are as comparable as possible to national CA registers, the most feasible solution was to exclude both metabolic and chromosomal disorders.

Extending the age for case ascertainment from age one to age five also resulted in discovering more than one CA diagnosis in the same child. Figure 19 plots the date of the first CA diagnosed in each child, and Figure 20, plots the date of the first CA diagnosed and the date of every other CA comorbidity diagnosed in the same child between the ages of 0 to 5 years. Figure 19 shows a cluster of points representing CA diagnoses around ages 0 to 1 years, but also a fairly consistent spread of CA diagnoses continuing between ages 1 to 5 years. Figure 20 demonstrates that the CA comorbidities diagnosed ages 0 to 5 years follow the same pattern as those described in Figure 19.

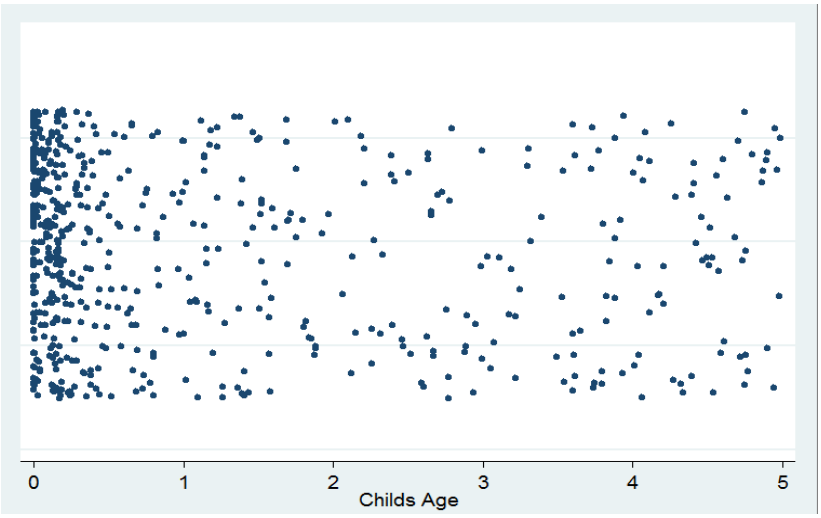


Figure 19: Scatter plot representing the date of diagnosis for each child's first CA in years

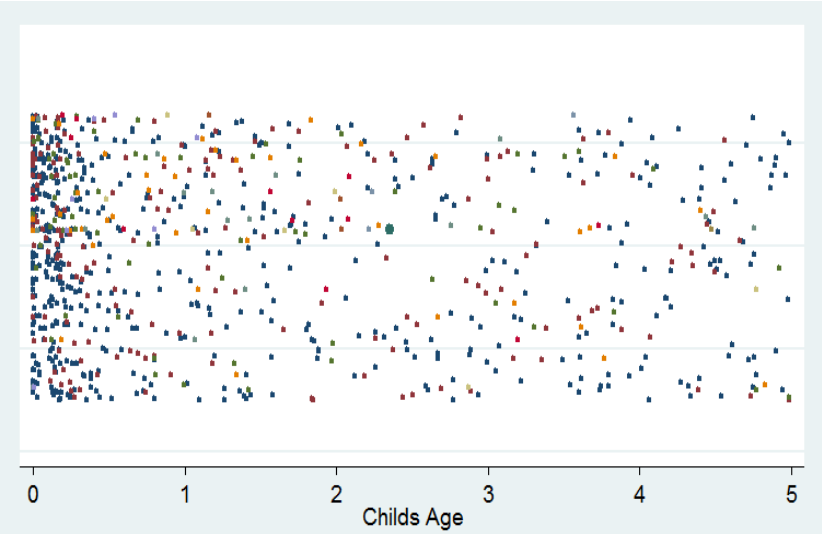


Figure 20: Scatter plot representing the date of diagnosis for all CA diagnosed per child in years

Figure 21 quantifies the number of children diagnosed with their first CA (excluding comorbidities) by age. Without the additional cases added from primary care data, this plot would only show the diagnoses made up to age 1 year, a total of 600 children. Primary care data adds a further 260 cases (30%).

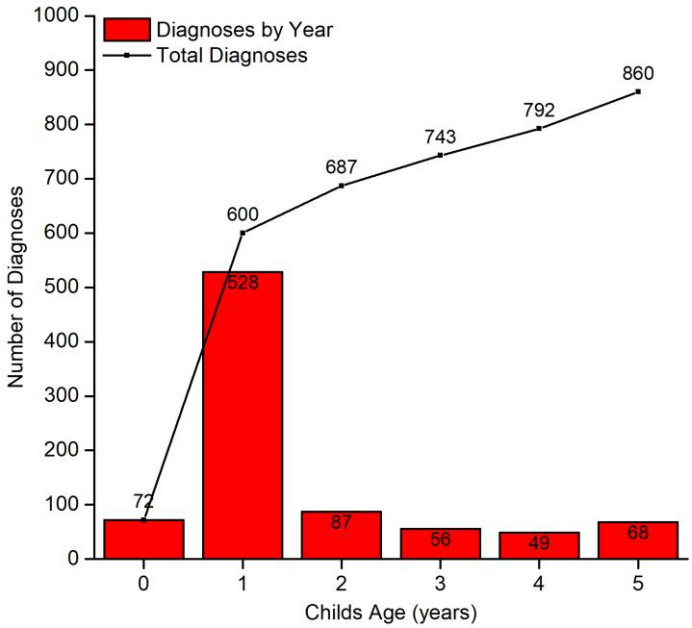


Figure 21: Total number of children diagnosed with a CA per year, and additional CA diagnoses made per year using the CA identified in phase 1 and phase 2 combined

4.1.3 CA case ascertainment by bodily system group

Further differences in CA case ascertainment are revealed when CA are categorised into bodily system group. As described in Section 3.4.4 of the methods, phase 1 (Sheridan et al. 2013) used BINOCAR guidelines from 2009. These report musculoskeletal (MSK) dysplasia's as a standalone subgroup. Study 1 reports CA rates according to BINOCAR's updated 2014 (2012 data) guidelines, which includes MSK conditions in the subgroup of 'other anomalies', a subgroup that also includes some genetic syndromes and skin disorders. Table 3 shows that prior to excluding metabolic and chromosomal disorders, the CA rates increase from 433 per 10,000 live births at age 0 to 1 years to 621 per 10,000 live births at ages 0 to 5 years, a percentage increase of 43%. Further percentage increases can be seen when comparing the CA discovered in each bodily system group for children aged up to one year and up to five years. The largest increase in CA diagnoses by category was for skeletal dysplasia's, which increased by 210%, followed by CA affecting the nervous system (129%) and respiratory CA (44%).

4.1.4 Characteristics of the BiB cohort

Table 4 describes the characteristics of mothers in the BiB cohort study that were used to identify maternal risk factors for CA. The risk factors were identified from the BiB baseline questionnaire data. The maternal risk factors included in the analysis were maternal age, ethnicity, BMI, maternal smoking, maternal education, IMD quintile, alcohol consumption during pregnancy and consanguinity (
Table 4). The data in
Table 4 includes mothers who gave birth to children with or without a CA, combining cases from both phase 1 and phase 2.

The ethnic origin of mothers is split between 40% white British mothers, 45% Pakistani mothers, and 15% mothers reporting different ethnicities, which is therefore referred to as 'Other' (
Table 4). The proportion of children with CA born to Pakistani mothers was higher than those born to mothers in the cohort overall (53% for Pakistani mothers, 47% for white British and other ethnicities combined). This pattern of mothers' ethnicities is similar to the findings of phase 1 (Sheridan et al. 2013), which reported the proportion of children with CA born to Pakistani mothers was higher than those born to mothers in the BiB cohort overall (60% vs 45%). Less than 1% of children with CA who were of white British origin were the offspring of first-cousin unions, compared to 49% of children with CA who were of Pakistani origin. There was a positive stepwise association between CA prevalence and the degree of consanguinity in the Pakistani subgroup: 9.5% of first-cousin progeny, 7.7% of second cousin progeny, 7.5% of beyond second cousins and 4.8% in non-consanguineous progeny. Seventy per cent of children with CA lived in areas defined by the IMD as the most deprived fifth of England (
Table 4). Proportionally more diagnoses of CA were recorded in children from non-consanguineous unions in phase 2 (424 CA), compared to children with CA from non-consanguineous unions in phase 1 (201 CA; Sheridan et al. 2013). This is an increase of 223 children, a 110% increase (
Table 4).

As mentioned in the methods section for study 1 (4.1.4), only mothers and their children with linked questionnaire data were included in the regression analyses, as the questionnaire data was used to determine risk factors for the analysis. There were 706 children with CA (Table 4) and questionnaire data, which also included children with metabolic and chromosomal disorders. The comparison group was 10,768 children without CA (Table 4).

describes the univariate and multivariable analyses of risk factors. The variables used in the analysis phase all had less than 1% missing data (
Table 4), apart from BMI, which had around 9% missing data across all ethnicities. Because of such a small amount of missing data, imputation was not required.

In the univariate model, smoking, BMI and drug use during pregnancy were not significant and so were not included in the multivariable model. Consanguinity to the first-cousin level was found to be a major risk factor for CA in Pakistani mothers (multivariable RR 1.87, 95% CI 1.46 to 2.38), as was maternal age >34 years, but only for mothers of 'other' ethnicities (multivariable RR 2.19, 95% CI 1.36 to 3.54). The previously reported association in phase 1 (Sheridan et al. 2013) between maternal education to degree level and a lower risk for CA persists for all ethnicities but, unlike phase 1 (Sheridan et al. 2013), is not significant when stratified by ethnicity (multivariable RR 0.78, 95% CI 0.62 to 0.98) (
). The results also show an increased risk of children born with CA to mothers in the least deprived IMD fifth overall, which was found in phase 1 (Sheridan et al. 2013) (
). When repeating the analyses at 99.9% CIs to address multiple testing, all the main effects remained significant (data not shown). No significant effect of interaction between IMD score and consanguinity was found for the risk of CA in the Pakistani population (Interaction RR 0.99, 95% CI 0.98 to 1.01).

		All	White British		Pakistani		Other	
	No CA	CA	No CA	CA	No CA	CA	No CA	CA
Ethnic origin	10768(94%)	706(6%)	4288(95%)	245(5%)	4804(93%)	371(7%)	1653(95%)	90(5%)
Age (years)								
20-34	8716(81%)	544(78%)	3231(75%)	180(73%)	4099(85%)	312(84%)	1366(83%)	62(69%)
<20	776(7%)	51(7%)	536(13%)	29(12%)	148(3%)	15(4%)	92(6%)	7(8%)
>34	1276(12%)	101(14%)	521(12%)	36(15%)	557(12%)	44(12%)	195(12%)	21(23%)
Missing	0	0	0	0	0	0	0	0
Education								
<5 GCSE equivalents	2304(21%)	172(24%)	856(20%)	52(21%)	1230(26%)	106(29%)	212(13%)	14(16%)
≥5 GCSE equivalents at grades A-C	3281(30%)	229(32%)	1457(34%)	85(35%)	1488(31%)	124(33%)	332(20%)	20(22%)
2 Advanced level equivalents	1561(15%)	96(14%)	731(17%)	37(15%0	604(13%)	49(13%)	224(14%)	10(11%)
Diploma, degree, or higher degrees	2775(26%)	145(21%)	826(19%)	45(18%)	1265(26%)	70(19%)	677(41%)	30(33%)
Other	590(5%)	45(6%)	372(9%)	22(9%)	144(3%)	17(5%)	74(4%)	6(7%)
Not Known	120(1%)	9(1%)	40(1%)	3(1%)	55(1%)	4(1%)	25(2%)	2(2%)
Foreign Unknown	110(1%)	8(1%)	3(<1%)	0	6(<1%)	0(<1%)	101(6%)	8(9%)
Missing	27(<1%)	2(<1%)	3(<1%)	1(<1%)	12(<1%)	1(<1%)	0	0
IMD 2010 score (fifths)								
1 (most deprived)	7124(66%)	491(70%)	2181(51%)	124(51%)	3812(79%)	299(81%)	1115(67%)	68(76%)

2	1949(18%)	116(16%)	925(22%)	54(22%)	688(14%)	49(13%)	332(20%)	13(14%)
3	1199(11%)	64(9%)	761(18%)	40(16%)	271(6%)	18(5%)	165(10%)	6(7%)
4	316(3%)	19(3%)	267(6%)	15(6%)	24(<1%)	2(<1%)	24(1%)	2(2%)
5 (least deprived)	177(2%)	16(2%)	152(4%)	12(5%)	8(<1%)	3(1%)	17(1%)	1(1%)
Missing	3(<1%)	0	2(<1%)	0	1(<1%)	0	0	0
Smoking								
No	8963(83%)	604(86%)	2842(66%)	160(65%)	4624(96%)	365(98%)	1479(89%)	79(88%)
Yes	1785(17%)	101(14%)	1444(34%)	84(34%)	167(3%)	6(2%)	172(10%)	11(12%)
Missing	20(<1%)	1(<1%)	2(<1%)	1(<1%)	13(<1%)	0	2(<1%)	0
Alcohol								
Yes	3311(31%)	184(26%)	2878(67%)	164(67%)	16(<1%)	0	410(25%)	20(22%)
No	7426(69%)	518(73%)	1403(33%)	81(33%)	4773(99%)	369(99%)	1238(75%)	68(76%)
Missing	31(<1%)	4(1%)	7(<1%)	0(<1%)	15(<1%)	2(<1%)	5(<1%)	2(2%)
Consanguinity *								
Non-consanguineous	7850(73%)	424(60%)	4284(99%)	244(99%)	2008(42%)	102(27%)	1538(93%)	78(87%)
First Cousin	1834(17%)	192(27%)	1(<1%)	1(<1%)	1753(36%)	183(49%)	79(5%)	8(9%)
Second cousin	637(6%)	55(8%)	0	1(<1%)	611(13%)	51(14%)	25(2%)	4(4%)
Other blood	447(4%)	35(5%)	3(<1%)	0	432(9%)	35(9%)	11(1%)	0
Missing	0	0	0	0	0	0	0	0
BMI								
Normal	4529(42%)	296(42%)	1738(41%)	87(36%)	2018(42%)	165(44%)	762(46%)	44(49%)
Overweight	2882(27%)	199(28%)	1141(27%)	65(27%)	1341(28%)	114(31%)	399(24%)	20(22%)
Obese	2126(20%)	122(17%)	992(23%)	54(22%)	856(18%)	51(14%)	273(17%)	17(19%)

Underweight	439(4%)	27(4%)	103(2%)	5(2%)	256(5%)	21(6%)	78(5%)	1(1%)
Missing	792(7%)	62(9%)	314(7%)	34(14%)	333(7%)	20(5%)	141(9%)	8(9%)
OGTT								
Normal	9850(91%)	637(90%)	4062(95%)	227(93%)	4261(89%)	328(88%)	1507(91%)	82(91%)
Impaired fasting glucose	33(<1%)	2(<1%)	6(<1%)	1(<1%)	18(<1%)	1(<1%)	8(<1%)	0
Impaired glucose tolerance	714(7%)	56(8%)	187(4%)	16(7%)	421(9%)	34(9%)	104(6%)	6(7%)
Diabetes	129(1%)	8(1%)	15(<1%)	1(<1%)	91(2%)	5(1%)	23(1%)	2(2%)
Missing	42(<1%)	3(<1%)	18(<1%)	0	13(<1%)	3(1%)	11(<1%)	0

Table 4: Demographics, lifestyle and clinical information of mothers in the Born in Bradford cohort who gave birth to children with or without a CA by ethnic group

*Coefficient of inbreeding values: F = 0 for Non-consanguineous, F = 0.0625, 0.0156 and <0.0156 for first cousin, second cousin and other blood respectively (Bittles 2012).

Univariate									**Multivariable**							
	All		White British		Pakistani		Other		All		White British		Pakistani		Other	
	RR (95% CI)	*p*	*RR* (95% CI)	*p*	*RR* (95% CI)	*p*	*RR* (95% CI)	*p*	*RR* (95% CI)	*p*	*RR* (95% CI)	*p*	*RR* (95% CI)	*p*	*RR* (95% CI)	*p*
Ethnic origin	1	-	1	-	1.33(1.13 to 1.55)	<0.0001	0.96(0.76 to 1.21)	0.70	-	-	-	-	-	-	-	-
Age(years)																
20-34	1	-	1	-	1	-	1	-	1	-	1	-	1	-	1	-
<20	1.01(0.76 to 1.34)	0.41	0.95(0.65 to 1.40)	0.81	1.23(0.74 to 2.05)	0.43	1.63(0.77 to 3.48)	0.20	1.08(0.81 to 1.44)	0.6	0.93(0.63 to 1.37)	0.71	1.23(0.73 to 2.05)	0.44	1.46(0.66 to 3.23)	0.35
>34	1.15(0.95 to 1.39)	0.16	1.04(0.74 to 1.45)	0.83	1.07(0.82 to 1.41)	0.61	1.99(1.19 to 3.34)	0.005	1.17(0.96 to 1.43)	0.12	1.01(0.71 to 1.42)	0.98	1.08(0.82 to 1.44)	0.58	2.19(1.36 to 3.54)	0.001
Education																
<5 GCSE equivalents	1	-	1	-	1	-			1	-	1	-	1	-	1	-
≥5 GCSE equivalents	0.94(0.78 to 1.14)	0.52	0.96(0.69 to 1.35)	0.82	0.97(0.76 to 1.24)	0.81	0.92(0.47 to 1.78)	0.80	1.00(0.82 to 1.21)	0.97	0.97(0.69 to 1.36)	0.84	1.00(0.77 to 1.28)	0.98	1.05(0.53 to 2.06)	0.9
Advanced level equivalents	0.83(0.65 to 1.06)	0.14	0.84(0.56 to 1.27)	0.41	0.95(0.68 to 1.31)	0.74	0.69(0.31 to 1.52)	0.36	0.92(0.71 to 1.18)	0.49	0.81(0.54 to 1.22)	0.32	1.00(0.71 to 1.41)	0.99	0.81(0.36 -1.85)	0.62
Diploma, or	0.71(0.58	0.00	0.90(0.61	0.6	0.66(0.49	0.01	0.68(0.37	0.23	0.78(0.62	0.03	0.86(0.56	0.5	0.74(0.54	0.05	0.80(0.41	0.53

higher degrees	to 0.89)	2	to 1.33)		to 0.89)		to 1.27)		to 0.98)		to 1.33)		to 1.00)		-1.58)	
Other	1.02(0.74 to 1.40)	0.9	0.98(0.60 to 1.58)	0.92	1.33(0.82 to 2.16)	0.25	1.21(0.48 to 3.04)	0.68	1.17(0.85 to 1.61)	0.35	0.98(0.60 to 1.60)	0.94	1.36(0.83 to 2.22)	0.22	1.33(0.53 to 3.30)	0.54
Don’t know	1.00(0.53 to 1.92)	0.99	1.22(0.40 to 3.75)	0.73	0.85(0.33 to 2.24)	0.75	1.20(0.29 to 4.98)	0.81	1.01(0.53 to 1.93)	0.98	1.28(0.41 to 3.94)	0.67	0.80(0.31 to 2.12)	0.66	1.52(0.39 to 6.04)	0.55
Foreign unknown	0.98(0.49 to 1.93)	0.94	0	<0.0001	0	<0.0001	1.18(0.51 to 2.74)	0.69	1.23(0.62 to 2.45)	0.56	0	0	0	<0.0001	1.47(0.62 to 3.50)	0.39
Alcohol																
No	1	-	1	-	1	-	1	-	1	-	1	-	1	-	1	-
Yes	0.81(0.69 to 0.95)	0.01	0.99(0.76 to 1.28)	0.93	0	<0.0001	0.89(0.55 to 1.45)	0.65	1.01(0.83 to 1.23)	0.91	0.98(0.76 to 1.27)	0.86	0	<0.0001	1.01(0.62 to 1.64)	0.96
Smoking																
No	1	-	1	-	1	-	1	-	-	-	-	-	-	-	-	-
Yes	0.85(0.69 to 1.04)	0.12	1.03(0.80 to 1.33)	0.81	0.47(0.21 to 1.05)	0.07	1.19(0.64 to 2.19)	0.59	-	-	-	-	-	-	-	-
Missing																
OGTT																
Normal	1	-	1	-	1	-	1	-	1	-	1	-	1	-	1	-
Impaired fasting glucose	0.94(0.24 to 3.62)	0.93	2.70(0.44 to 16.65)	0.28	0.74(0.11 to 4.98)	0.75	0	<0.0001	0.46(0.07 to 3.12)	0.43	1.56(0.54 to 4.51)	0.42	0	<0.0001	0	<0.0001
Impaired	1.20(0.92	0.18	1.49(0.91	0.11	1.05(0.74	0.8	1.06(0.47	0.89	1.12(0.86	0.41	1.50(0.92	0.1	1.01(0.72	0.95	0.97(0.43	0.94

glucose tolerance	to 1.56)		to 2.42)		to 1.47)		to 2.37)		to 1.46)		to 2.46)		to 1.43)		to 2.18)	
Diabetes	0.96(0.49 to 1.89)	0.91	1.18(0.18 to 7.91)	0.86	0.73(0.31 to 1.72)	0.47	1.55(0.40 to 5.96)	0.52	0.85(0.43 to 1.69)	0.65	1.21(0.18 to 8.17)	0.84	0.72(0.30 to 1.72)	0.46	1.14(0.29 to 4.49)	0.86
IMD 2010 score																
1(most deprived)	1	-	1	-	1	-	1	-	1	-	1	-	1	-	1	-
2	0.87(0.72 to 1.06)	0.17	1.03(0.75 to 1.40)	0.88	0.91(0.68 to 1.22)	0.55	0.66(0.37 to 1.17)	0.15	0.96(0.78 to 1.18)	0.7	1.02(0.74 to 1.40)	0.93	0.99(0.74 to 1.33)	0.95	0.66(0.37 to 1.21)	0.2
3	0.79(0.61 to 1.01)	0.06	0.93(0.66 to 1.31)	0.67	0.86(0.54 to 1.36)	0.51	0.61(0.27 to 1.39)	0.24	0.89(0.68 to 1.17)	0.41	0.92(0.63 to 1.34)	0.67	0.99(0.62 to 1.58)	0.97	0.41(0.14 to 1.16)	0.94
4	0.88(0.56 to 1.37)	0.57	0.99(0.59 to 1.67)	0.97	1.06(0.28 to 4.02)	0.93	1.34(0.35 to 5.17)	0.67	1.11(0.70 to 1.76)	0.66	1.02(0.59 to 1.75)	0.95	1.64(0.45 to 6.02)	0.45	1.30(0.39 to 4.34)	0.67
5(least deprived)	1.29(0.80 to 2.07)	0.3	1.36(0.77 to 2.41)	0.29	3.75(1.42 to 9.90)	0.01	0.97(0.14 to 6.59)	0.97	1.66(1.01 to 2.71)	0.05	1.41(0.77 to 2.57)	0.26	4.93(1.77 to 13.73)	0.002	0.97(1.15 to 6.45)	0.98
Consanguinity																
Non-consanguineous	1	-	1	-	1	-	1	-	1	-	1	-	1	-	1	-
1st cousin	1.85(1.57 to 2.18)	<0.000	9.28(2.31 to 37.30)	0.002	1.96(1.55 to 2.47)	<0.0001	1.91(0.95 to 3.82)	0.07	1.82(1.50 to 2.20)	<0.000	6.87(1.68 to 23.18)	0.01	1.87(1.46 to 2.38)	<0.0001	1.79(0.86 to 3.74)	0.12

		1								1						
Second cousin	1.55(1.18 to 2.03)	0.001	1	-	1.59(1.15 to 2.20)	0.005	2.86(1.12 to 7.28)	0.028	1.58(1.19 to 2.10)	0.002	0	-	1.54(1.11 to 2.15)	0.009	3.33(1.27 to 8.73)	0.015
Other blood	1.42(1.02 to 1.98)	0.04	0	<0.001	1.55(1.07 to 2.25)	0.02	0	<0.001	1.44(1.03 to 2.03)	0.35	0	<0.001	1.53(1.06 to 2.21)	0.024	0	<0.001
BMI																
Normal	1	-	1	-	1	-	1	-	1	-	1	-	-	-	-	-
Overweight	1.05(0.88 to 1.25)	0.56	1.13(0.83 to 1.55)	0.44	1.04(0.82 to 1.30)	0.76	0.87(0.52 to 1.46)	0.61	-	-	-	-	-	-	-	-
Obese	0.88(0.72 to 1.09)	0.24	1.08(0.78 to 1.51)	0.64	0.74(0.55 to 1.01)	0.06	1.07(0.62 to 1.85)	0.8	-	-	-	-	-	-	-	-
Underweight	0.94(0.64 to 1.38)	0.77	0.97(0.40 to 2.34)	0.95	1.00(0.65 to 1.55)	0.99	0.23(0.03 to 1.66)	0.15	-	-	-	-	-	-	-	-
Missing																
Drugs																
Total drugs 1st trimester or 3 months before																
No	-	-	-	-	-	-	-	-								
Yes	1.01(0.87 to 1.16)	0.918	0.99(0.77 to 1.27)	0.94	0.94(0.78 to 1.15)	0.56	1.09(0.71 to 1.65)	0.70								
Psychotic																

drugs in pregnancy								
No	-	-	-	-	-	-	-	-
Yes	1.07(0.77 to 1.49)	0.67	1.18(0.74 to 1.87)	0.50	1.01(0.60 to 1.68)	0.98	1.19(0.39 to 3.64)	0.76

Table 5: Univariate and multivariable RR of CA related to demographic, lifestyle and clinical risk factors in the BiB cohort by ethnic group

4.2 Results of study 2

The results of the healthcare use analysis are reported as described in Section 3.5 of the methods, and structured in this section as follows. Healthcare use in terms of the use of hospital services, primary care consultations, and referrals to specialists are reported. First, descriptive statistical analysis for the healthcare use of children with CA compared to children without CA in the BiB cohort is presented. Second, the results of a statistical analysis that used three different outcomes are reported. These outcomes were hospital episode statistics, primary care consultations, and referrals to multidisciplinary specialists. For each outcome, three different models are used. First, model 1 is a univariate model testing the association between each healthcare use outcome and children in the BiB cohort in turn. Model 2 is a multivariable model that adjusts for confounders determined to affect the uptake of healthcare; confounders that were explored in Section 2.5.3 of the literature review and in the DAGs in Section 3.5.4 of the methods. Model 3 adjusts for both confounders and measures of underlying ill health.

4.2.1 Describing healthcare use for children with CA

The characteristics of mothers who gave birth to children with a CA, linked to BiB questionnaire data (CA = 706, no CA = 10768), are described in Table 6. The average number of times a child used hospital services and primary care consultations per year up to the child's fifth birthday, for children with and without CA, are also described in Table 6. Hospital events included admissions for elective procedures, other emergencies and A & E presentations.

	All		**White British**		**Pakistani**		**Other**	
	No CA	CA	No CA	CA	No CA	CA	No CA	CA
Ethnic origin	10768 (93.85%)	706(6.15%)	4288(94.60%)	245(5.40%)	4804(92.83%)	371(7.17%)	1653(94.84%)	90(5.16%)
Economic deprivation								
Economically deprived	6147(57.09%)	444(62.89%	2072(48.32%)	116(47.35%)	3315(69.00%	280(75.47%)	758(45.86%)	48(53.33%)
Not economically deprived	4166(38.69%)	247(34.99%)	2034(47.43%)	122(49.80%)	1340(27.89)%	85(22.91%)	792(47.91%)	40(44.44%)
Missing	455(4.23%)	15(2.12%)	182(4.24%)	7(2.86%)	149(3.10%)	6(1.62%)	103(6.23%)	2(2.22%)
Age of mother								
20-34	8716(80.94%)	554(78.47%)	3231(75.35%)	180(73.47%)	4099(85.32%)	312(84.10%)	1366(82.64%)	62(68.89%)
<20	776(7.21%)	51(7.22%)	536(12.50%)	29(11.84%)	148(3.08%)	15(4.04%)	92(5.57%)	7(7.78%)
>34	1276(11.85%)	101(14.31%)	521(12.15%)	36(14.69%)	557(11.59)	44(11.86%)	195(11.80%)	21(23.33%)
Consanguinity								
Non-consanguineous	7850(72.90%)	424(60.06%)	4284(99.81%)	224(99.59%)	2008(41.80%)	102(27.49%)	1538(93.04%)	78(86.67%)
First Cousin	1834(17.03%)	192(27.20%)	1(<1%)	1(<1%)	1753(36.49%)	183(49.33%)	79(4.78%)	8(8.89%)
Second Cousin	637(5.92%)	55(7.79%)	0	0	611(12.72%)	51(13.75%)	25(1.51%)	4(4.44%)
Other blood	447(4.15%)	35(4.96%)	3(<1%)	0	432(8.99%)	35(9.43%)	11(0.67%)	0
Maternal Education								
Lower education	2894(26.88%)	217(30.74%	1228(28.64%)	74(30.20%)	1374(28.60%)	123(33.15%)	286(17.30%)	20(22.22%)
Higher education	7617(70.74%)	470(66.57%)	3014(70.29%)	167(68.16%)	3357(69.88%)	243(65.50%)	1223(74.59%)	60(66.67%)

Healthcare use of children								
Average GP appointments per year	5.21	6.82	4.21	5.49	6.20	7.89	4.91	6.01
Average hospital admissions per year	0.11	0.50	0.11	0.32	0.12	0.60	0.08	0.60

Table 6: Demographics, lifestyle and clinical information of Born in Bradford mothers who gave birth to a child with CA by ethnic group, and healthcare use of children with CA

Children of Pakistani origin with CA had on average 1.69 more primary care consultations, and 0.48 more hospital admissions per year than children without CA (Table 6). Children with CA of Pakistani origin had the highest number of primary care consultations over the five-year period, with on average 2.4 more primary care appointments per year than children of white British origin. The most common reason for use of hospital services for children in general, whether they had a CA or not, was respiratory conditions. When stratified by the type of hospital admission, children with CA had more 'other emergency' admissions (40%), followed by elective admissions (34%). Children without CA on the other hand, had the most Accident & Emergency (49%) admissions (Table 7).

The diagnoses recorded at the time of admission were also different for children with CA compared to children without CA. Although respiratory conditions were the most common cause of A&E admissions and other emergency admissions for both children with and without CA, neoplasms, blood and immune system disorders were the most common reason for elective hospital admissions for children with CA, and eye and ear conditions were the most common reason for elective hospital admissions for children without CA.

Figure 22 summarises the results of the medical record review and the different multidisciplinary healthcare professionals that children with CA are referred to. A total of 41 different healthcare professionals were identified as receiving referrals for children with CA. The most common referral was received by consultant paediatricians (14%), followed by neonatologists (13%), paediatric surgeons (8%) and cardiologists (7%). On average, children had between three and four different healthcare professionals involved in their care at any one time.

Admittance type	Total number of hospital admissions over 5 years		Most common reason for admission	
	No CA	CA	No CA	CA
A&E	3985(49%)	609(26%)	1. Respiratory 2. Injury/poison	1. Respiratory system 2. Infectious parasitic
Other Emergency	2522(31%)	932(40%)	1. Respiratory system 2. Infectious parasitic	1. Respiratory system 2. Clinical lab findings
Elective	1632(20%)	801(34%)	1. Eye/ear 2. Respiratory system	1. Neoplasms/blood/immune 2. Congenital abnormalities

Table 7: Proportion of hospital admissions by admission type and most common reason for admission to hospital

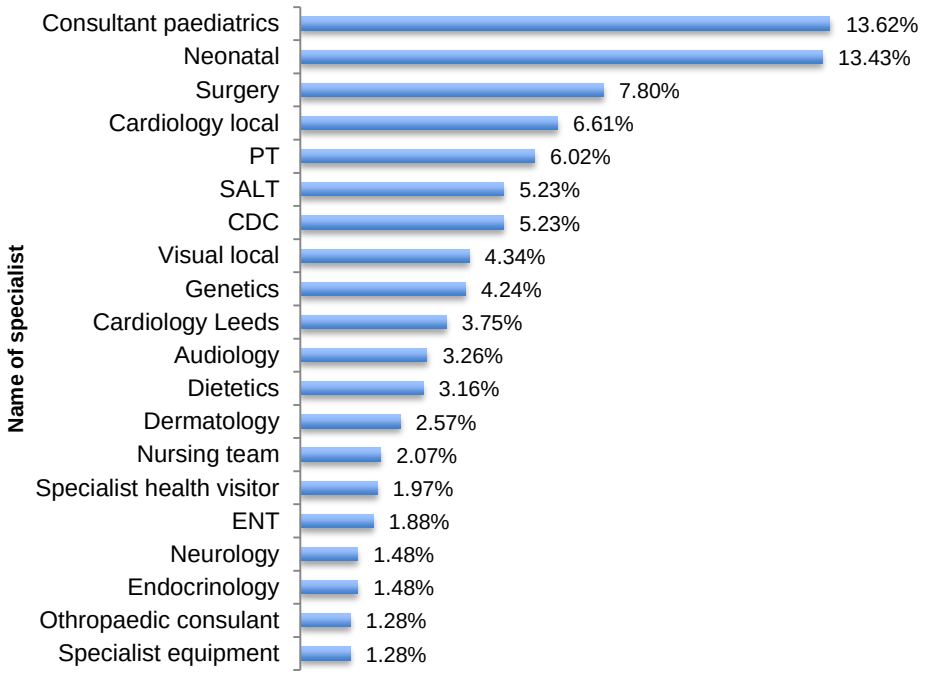


Figure 22: The top 20 most frequently referred to healthcare specialists from a total of 41 multidisciplinary specialists

4.2.2 Risk factors for healthcare use

Table 8 reports the incident rate ratios for models 1 to 3 for the outcomes of primary care consultations and use of hospital services, and children in the BiB cohort as the exposure. Both models 1 and 2 show that children from economically deprived neighbourhoods have an increased use of hospital services (multivariate IRR, 1.41, 95% CI 1.31 to 1.52), but do not have an increased use of primary care consultations (multivariable IRR, 1.01, 95% CI 0.98 to 1.04). When considering model 3, which adjusts for ill health, this increase in use of hospital services seen for children from economically deprived neighbourhoods reduces (multivariable IRR, 1.15, 95% CI 1.07 to 1.24). Interaction effects between whether the child had a CA and economic deprivation were not found to be significant.

Children from both Pakistani (multivariate IRR, 1.50, 95% CI 1.44 to 1.56) and other ethnicities (multivariable IRR, 1.29, 95% CI 1.23 to 1.35) had an increase in primary care consultations in both models 1 and 2, which again reduced after controlling for ill health in model 3 (Table 8). Children who had older mothers (>34) were predicted to use hospital services less (multivariable IRR, 0.84, 95% CI 0.75 to 0.94), but this reduction in healthcare use was not seen for primary care consultations in model 2 after adjusting for confounders (multivariable IRR, 0.97, 95% CI 0.92 to 1.01). The reduction in the use of hospital services for children who had older mothers (>34) did not change significantly after controlling for ill health in model 3 (multivariable IRR, 0.84, 95% CI 0.76 to 0.93).

Children born from consanguineous unions at the first-cousin level had an increased use of hospital services in model 2 (multivariate IRR, 1.33, 95% CI 1.19 to 1.48), but not primary care consultations (multivariate IRR, 1.03 95% CI 0.99 to 1.08). This increase in the use of hospital services reduced slightly after controlling for ill health in model 3 (multivariate IRR 1.23, 95% CI 1.11 to 1.36). The most significant increase in healthcare use was observed for children with CA, for which the use of hospital services (multivariate IRR, 4.38, 95% CI 3.90

to 4.92) was three times higher than primary care use (multivariate IRR, 1.27, 95% CI 1.20 to 1.35) after adjusting for confounders (Table 8). For children that had mothers with higher educational levels (degree level), both use of primary care (multivariate IRR, 0.96, 95% CI 0.93 to 1.00) and use of hospital services reduced (multivariate IRR, 0.91 95% CI 0.84 to 0.98) (Table 8).

For the regression analysis exploring multidisciplinary referrals, more referrals to different healthcare professionals were seen for children with CA compared to children without CA, after adjustment for confounders in model 2 (multivariate β, 3.59, 95% CI 3.11 to 4.08). In model 3, after adjusting for ill health, the predicted increased use of multidisciplinary referrals for children with CA reduces (multivariable β, 2.27, 95% CI 1.59 to 2.94) (Table 9,

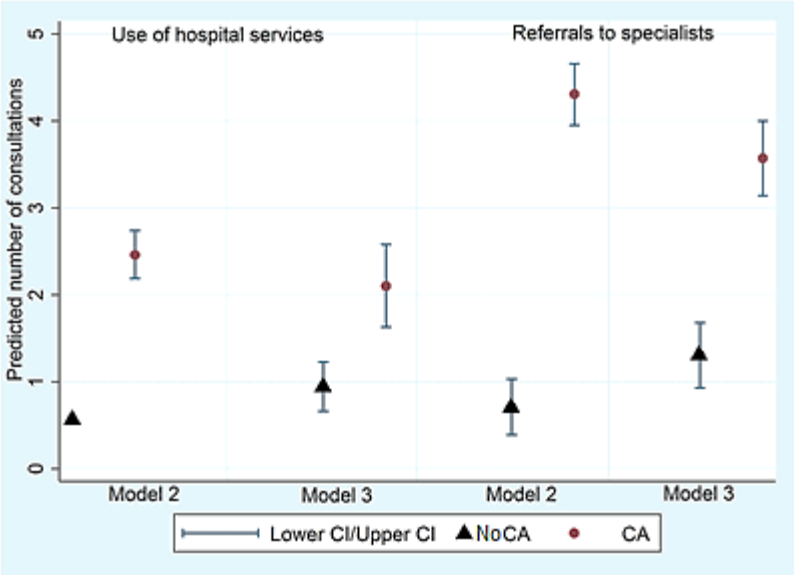
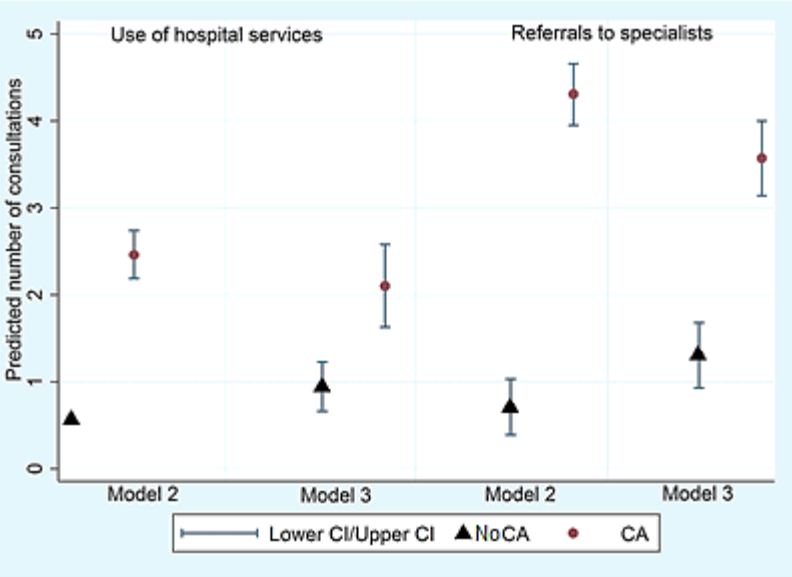


Figure 23). The only other marginally significant factor was a slight increase in referrals to multidisciplinary specialists for children born into economically deprived neighbourhoods after adjustment for confounders in model 2 (multivariable β, 0.55, 95% CI 0.01 to 1.09).

The services with the highest predicted use for children in the BiB cohort were hospital services and multidisciplinary referrals. The marginal effect sizes for

both models 2 and 3 for children with CA compared to children without CA are plotted in



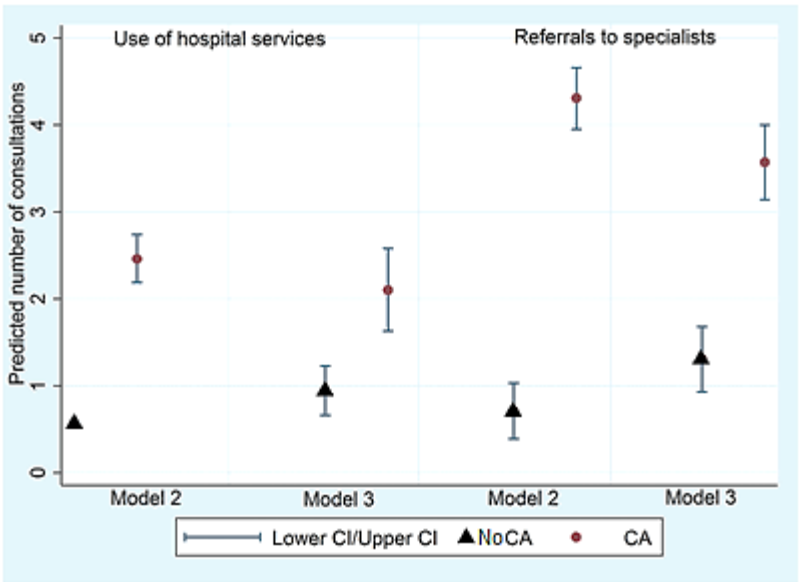


Figure 23.

Figure 23 shows that after controlling for ill health in model 2, the predicted increased use of hospital services for children with CA reduces by almost half, but still remains (multivariable IRR 2.23, 1.88 to 2.65). For referrals to multidisciplinary specialists, the rate also reduced (β 2.27, 95% CI 1.59 to 2.94).

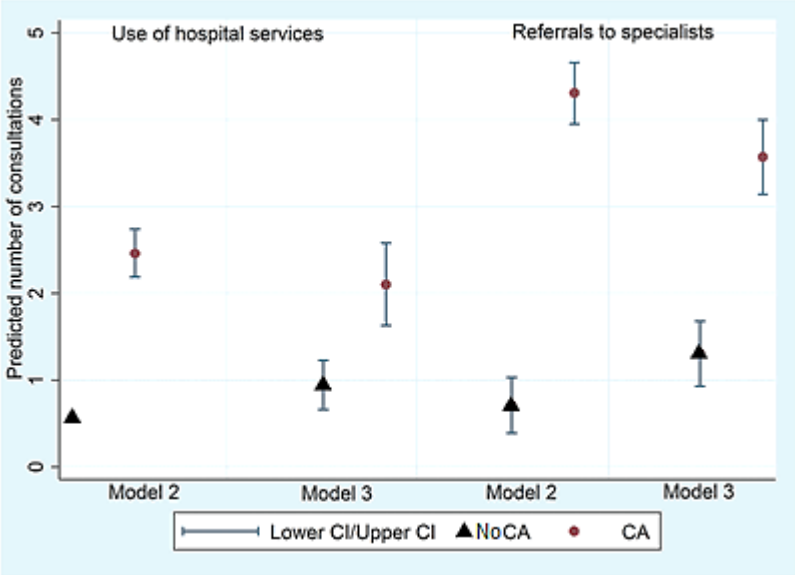


Figure 23: Predicted use of hospital services and referrals to multidisciplinary specialists for children with and without CA

* Model 2: Multivariable, Model 3: Adjusted for ill health

	Outcome 1: Primary care consultations						Outcome 2: Use of hospital services					
	Model 1: Univariate		Model 2: Multivariable		Model 3: Adjusted for underlying ill health		Model 1: Univariate		Model 2: Multivariable		Model 3: Adjusted for underlying ill health	
	IRR	*p*	*IRR*	*p*	*IRR*	*p*	*IRR*	*P*	*IRR*	*p*	*IRR*	*p*
	(95% CI)		*(95% CI)*		*(95% CI)*		*(95% CI)*		*(95% CI)*		*(95% CI)*	
Economic deprivation												
Economically deprived	1.12(1.08 to 1.15)	<0.0001	1.01(0.98 to 1.04)	0.48	0.98(0.95 to 1.00)	0.06	1.41(1.31 to 1.52)	<0.0001	1.24(1.14 to 1.34)	<0.0001	1.15(1.07 to 1.24)	<0.0001
Not Economically deprived												
Ethnicity												
White British	-	-	-	-	-	-	-	-	-	-	-	-
Pakistani	1.53(1.49 to 1.59)	<0.0001	1.50(1.44 to 1.56)	<0.0001	1.29(1.25 to 1.34)	<0.0001	1.31(1.21 to 1.41)	<0.0001	0.98(0.89 to 1.08)	0.64	0.82(0.75 to 0.90)	<0.0001
Other	1.28(1.22 to 1.33)	<0.0001	1.29(1.23 to 1.35	<0.0001	1.17(1.12 to 1.21)	<0.0001	0.92(0.92 to 1.03)	0.15	0.87(0.78 to 0.97)	0.02	0.75(0.67 to 0.84)	<0.0001
Mothers age												
20-34	-	-	-	-	-	-			-	-	-	-
<20	0.88(0.83 to 0.92)	<0.0001	0.99(0.94 to 1.04)	0.69	1.03(0.98 to 1.07)	0.29	1.11(0.97 to 1.28)	0.13	1.07(0.94 to 1.23)	0.32	1.12(0.99 to 1.28)	0.07

>34	0.95(0.90 to 0.99)	0.02	0.97(0.92 to 1.01)	0.12	0.95(0.91 to 0.98)	0.005	0.86(0.77 to 0.96)	0.01	0.84(0.75 to 0.94)	0.002	0.84(0.76 to 0.93)	0.001
Consanguinity												
Non-consanguineous	-	-	-	-	-	-	-	-			-	-
First cousin	1.33(1.29 to 1.39)	<0.0001	1.03(0.99 to 1.08)	0.16	0.98(0.94 to 1.01)	0.22	1.62(1.48 to 1.78)	<0.0001	1.33(1.19 to 1.48)	<0.0001	1.23(1.11 to 1.36)	<0.0001
Second cousin	1.26(1.20 to 1.35)	<0.0001	0.99(0.93 to 1.06)	0.79	0.98(0.93 to 1.03)	0.45	1.27(1.09 to 1.47)	0.002	0.99(0.85 to 1.17)	0.94	0.94(0.81 to 1.10)	0.47
Other blood	1.28(1.20 to 1.38)	<0.0001	1.01(0.93 to 1.08)	0.86	1.00(0.94 to 1.07)	0.93	1.36(1.15 to 1.62)	<0.0001	1.26(1.05 to 1.50)	0.01	1.16(0.98 to 1.38)	0.08
Congenital Anomaly												
Yes	1.34(1.26 to 1.42)	<0.0001	1.27(1.20 to 1.35)	<0.0001	1.24(1.15 to 1.34)	<0.0001	4.32(3.89 to 4.81)	<0.0001	4.38(3.90 to 4.92)	<0.0001	2.23(1.88 to 2.65)	<0.0001
No	-	-		-	-	-	-	-	-	-	-	-
Maternal Education												
Lower education	-	-	-	-	-	-	-	-	-	-	-	-
Higher education	0.96(0.93 to 0.99)	0.007	0.96(0.93 to 1.00)	0.03	0.98(0.95 to 1.01)	0.11	0.81(0.75 to 0.87)	<0.0001	0.91(0.84 to 0.99)	0.02	0.93(0.86 to 1.01)	0.07

Table 8: Univariate and multivariable predicted rates of primary care consultations and use of hospital services adjusted for demographic and lifestyle factors

Outcome 3: Referrals

	Model 1: Univariate		Model 2: Multivariable		Model 3: Adjusted for underlying ill health	
	Coefficient	*p*	*Coefficient*	*p*	*Coefficient*	*p*
	(95% CI)		*(95% CI)*		(95% CI)	
Economic deprivation						
Economically deprived	0.95(0.35 to 1.56)	0.002	0.55(0.01 to 1.09)	0.05	0.37(-0.16 to 0.86)	0.18
Not Economically deprived	-	-	-	-	-	-
Ethnicity						
White British	-	-	-	-	-	-
Pakistani	0.72(0.09 to 1.36)	0.003	-0.27(-0.95 to 0.39)	0.42	-0.34(0.98 to 0.29)	0.29
Other	-0.03(-0.92 to 0.85)	0.94	-0.36(-1.11 to 0.39)	0.35	-0.38(-1.09 to 0.33)	0.29
Mothers age						
20-34	-	-	-	-	-	-
<20	-0.31(-1.39 to 0.77	0.58	-0.42(-1.32 to 0.48)	0.36	-0.32(-1.17 to 0.52)	0.45
>34	0.83(-0.08 to 1.74)	0.07	0.64(-0.10 to 1.37)	0.09	0.50(-0.20 to 1.19)	0.16
Consanguinity						
Non-consanguineous	-	-	-	-	-	-
First cousin	1.19(0.48 to 1.91)	0.001	0.24(-0.50 to 0.97)	0.52	0.10(-0.61 to 0.80)	0.79

Second cousin	1.17(0.11 to 2.23)	0.031	0.26(-0.70 to 1.21)	0.59	0.42(-0.49 to 1.32)	0.37
Other blood	-0.03(-1.54 to 1.48)	0.96	-0.32(-1.60 to 0.97)	0.63	-0.98(-2.22 to 0.25)	0.12
Congenital Anomaly						
Yes	3.71(3.28 to 4.15)	<0.0001	3.59(3.11 to 4.08)	<0.0001	2.27(1.59 to 2.94)	<0.0001
No	-	-	-	-	-	-
Maternal Education						
Lower education	-	-	-	-	-	-
Higher education	-0.70(-1.34 to 0.06)	0.032	0.05(-0.47 to 0.57)	0.86	-0.14(-0.66 to 0.38)	0.60

Table 9: Univariate and multivariable predicted rates of referrals to multidisciplinary specialists adjusted for demographic and lifestyle factors

Table 10 reports the results of the healthcare use regression analysis, which stratifies the exposure for children with and without CA. The multivariable regression outputs are reported for each healthcare use outcome. For primary care consultations and the use of hospital services, relative risks (RR) are reported, and for the multidisciplinary referrals analysis, coefficients are reported. This regression analysis revealed that children of Pakistani origin had a relatively similar use of primary care consultations whether they had a CA (multivariable RR, 1.42, 95% CI 1.19 to 1.69) or not, albeit slightly higher for children without CA (multivariable RR, 1.50, 95% CI 1.44 to 1.56). For use of hospital services, children of Pakistani origin were more likely to use hospital services if they had a CA (multivariable RR, 1.79, 95% CI 1.26 to 2.52) compared to children without a CA (multivariable RR, 0.92, 95% CI 0.84 to 1.02). Children from economically deprived neighbourhoods with CA had very similar use of hospital services (multivariable RR, 1.34, 95% CI 1.03 to 1.75) compared to those without CA (multivariable RR, 1.23, 95% CI 1.13 to 1.33). Children with CA whose mothers had a higher education level (to degree level) used more primary care consultations (multivariable RR, 1.02, 95% CI 0.90 to 1.16). The same result for hospital services was found but this was not significant (multivariable RR, 0.90, 95% CI 0.70 to 1.17). For the referral analyses, children with CA whose mothers were older (>34) had an increased risk of referrals to multidisciplinary specialists (β 1.74, 95% CI 0.16 to 3.31). No other results from the referral analyses were significant.

	Outcome 1: Primary Care consultation				Outcome 2: Use of hospital services				Outcome 3: Referrals			
	CA		No CA		CA		No CA		CA		No CA	
Ethnic origin	*RR (95% CI)*	*p*	*RR (95% CI)*	*p*	*RR (95% CI)*	*p*	*RR (95% CI)*	*p*	*Coefficient (95% CI)*	*p*	*Coefficient (95% CI)*	*p*
White British	-	-	-	-	-	-	-	-	-	-	-	-
Pakistani	1.42(1.19 to 1.69)	<0.0001	1.50(1.44 to 1.56)	<0.0001	1.79(1.26 to 2.52)	<0.0001	0.92(0.84 to 1.02)	0.13	-0.83(-2.43 to 0.78)	0.31	-0.02(-0.41 to 0.36)	0.90
Other	1.20(0.99 to 1.45)	0.067	1.29(1.24 to 1.36)	<0.0001	0.80(0.45 to 1.44)	0.47	0.80(0.71 to 0.90)	<0.0001	-0.53(-2.30 to 1.24)	0.56	-0.33(-0.78 to 0.12)	0.15
Economic deprivation												
Economically deprived	1.00(0.88 to 1.12)	0.95	1.01(0.98 to 1.05)	0.44	1.34(1.03 to 1.75)	0.03	1.23(1.13 to 1.33)	<0.0001	0.94(-0.30 to 2.17)	0.14	0.42(0.10 to 0.74)	0.01
Not economically deprived	-	-	-	-	-	-	-	-	-	-		
Age of mother												
20-34	-	-	-	-	-	-	-	-	-	-	-	-
<20	1.03(0.82 to 1.28)	0.82	0.99(0.93 to 1.05)	0.67	1.29(0.83 to 2.00)	0.27	1.03(0.89 to 1.19)	0.70	-0.48(-2.41 to 1.46)	0.63	-0.28(-0.85 to 0.28)	0.32
>34	0.92(0.77 to 1.10)	0.34	0.97(0.93 to 1.02)	0.20	0.89(0.63 to 1.24)	0.48	0.84(0.74 to 0.95)	0.004	1.74(0.16 to 3.31)	0.03	-0.16(-0.61 to 0.30)	0.49
Consanguinity												
First Cousin	1.19(1.00	0.41	1.02(0.97	0.40	1.08(0.76	0.67	1.35(1.21	<0.0001	0.92(-0.62	0.24	-0.21(-0.69	0.38

	to 1.41)		to 1.07)		to 1.53)		to 1.52)		to 2.47)		to 0.27)	
Second cousin	1.04(0.82 to 1.31)	0.77	0.99(0.93 to 1.06)	0.77	1.14(0.72 to 1.83)	0.57	0.95(0.80 to 1.13)	0.54	0.58(-1.29 to 2.45)	0.54	0.28(-0.38 to 0.95)	0.40
Other blood	1.34(1.01 to 1.77)	0.04	0.99(0.91 to 1.06)	0.04	0.81(0.45 to 1.44)	0.47	1.31(1.09 to 1.58)	0.004	0.24(-2.43 to 2.92)	0.86	-0.58(-1.39 to 0.24)	0.16
Maternal Education												
Lower education	-	-	-	-	-	-	-	-	-	-	-	-
Higher education	1.02(0.90 to 1.16)	0.02	0.96(0.93 to 0.99)	0.75	0.90(0.70 to 1.17)	0.44	0.91(0.84 to 0.99)	0.03	0.22(-0.91 to 1.36)	0.70	-0.03(-0.38 to 0.32)	0.88

Table 10: Multivariable predicted rates of healthcare use by type of healthcare use, for children with and without CA

5 Discussion

5.1 Chapter overview

This chapter addresses research objective number 4, and discusses the prevalence study and investigation of healthcare use in terms of their implications for improving current healthcare services for children with complex healthcare needs. This discussion focuses on the key results from each study, and includes an overview of how the methodologies adopted contribute to current knowledge for ascertaining the prevalence of children with complex healthcare needs, and their impact on healthcare. There are design limitations and these, along with key learning points are discussed to inform future studies of this kind.

Section 5.2 discusses the key findings from study 1, in terms of their contribution to assessing the benefits of using primary care data as a method for CA case ascertainment, how extending the age for case ascertainment effects the type of CA detected in children by bodily system group, and how the impact of children with complex healthcare needs on healthcare systems may be underestimated as a result of not extending the age of case ascertainment.

Section 5.3 discusses the key findings from study 2 and reflects on the potential value of quantifying the impact that children with complex healthcare needs have on the healthcare service, how data linkage facilitates our understanding of healthcare use for complex diseases which require input from a range of different services, and how other modifiable factors in addition to ill health can affect healthcare use.

Section 5.4 summarises the concomitant elements of both studies, how they complement each other and present a defined methodology for ascertaining, and exploring the healthcare use of people with complex diseases.

5.2 Key findings from study 1

Study 1 combined prospectively ascertained primary care data, with detailed maternal clinical, social and environmental risk information from a large ongoing birth cohort study to produce new estimates of CA prevalence and identified cases that were used in study 2. Central to doing this was the ability to perform data linkage using a unique identifier, in this case NHS number. The following key findings relating to CA case ascertainment were made:

1. Primary care data is a valid and useful source for ascertaining CA prevalence.
2. Continuing case attainment up to age five detects previously under-ascertained cases of CA in the BiB population, from 432.9 per 10,000 live births at age one to 620.6 at age five.
3. Without accurate case ascertainment it is likely that both general and specialist services for CA will be under-resourced.
4. Compared to the phase 1 CA study (Sheridan et al. 2013), some similarities and changes in risk patterns are evident when considering cases up to age five:
    - Consanguinity remains the most significant risk factor in the Pakistani community
    - Maternal age >34 years remains a significant risk factor for other ethnicities
    - The previously reported association between maternal education to degree level and a lower risk for CA persists for all ethnicities but, unlike phase 1 (Sheridan et al. 2013), is not significant when stratified by ethnicity.

5.2.1 CA case ascertainment

In 2011, the Chief Medical Officer proposed that PHE must ensure nationwide coverage of CA registers, and endorse cost-effective methods of surveillance using existing information systems for the combined benefits of patients, commissioners and clinicians (DH 2011). Choosing children with CA as an exemplar for children with complex healthcare needs, while originally designed as a method for ascertaining a study population linked to healthcare use data, also catalysed a major finding relevant for CA research. One of the most impactful findings in this thesis was the discovery of an additional 30% of CA cases found when using primary care data and expanding the age for case ascertainment. While also relevant to CA case ascertainment methods, this finding also highlights that the impact of children with complex healthcare needs on the healthcare service is likely to be much higher than previously thought.

In the most recent BINOCAR (2014) CA report, which uses data from 2012, less than 2% of live births were diagnosed after one year of age. Using primary care data for children aged 0 to 5 years, study 1 observed rates of CA was almost twice those that were previously reported in phase 1 (Sheridan et al. 2013). The choice of using primary care data and extending the age for CA case ascertainment to children aged 0 to 5 years, revealed that only 70% of diagnoses in study 1 were made prior to the child's first birthday.

This is a major finding, and as such, several attempts were made in this thesis to ensure the CA cases that were extracted were genuine cases, rather than errors in the primary care data. As well as the validation of CA cases using appropriate coding methods and comparing different approaches to data extraction, addressed in Section 3.4.5, there are other validation steps made possible through comparisons to previous CA research. In chapter 2, several studies were identified in the literature, which discussed the potential of primary care data for CA case ascertainment

(Charlton et al. 2010; Sokal et al. 2013; Wurst et al. 2007a; Wurst et al. 2007b; Devine et al. 2008; Sokal et al. 2014; Hammad et al. 2013).

One of these studies in particular, which used another UK database of primary care records (THIN), reported very similar findings to those of this thesis (Sokal et al. 2013). They discovered that that 72% (70% in this thesis), of CA diagnosed up to age one year, and when including the remaining 28% of CA (using a median of 6.7 years follow-up), the CA rate increased from 198 per 10,000 live births, to 277 per 10,000 live births (Sokal et al. 2013), a percentage increase of 14%. In this thesis, study 1 found 70% of CA was diagnosed up to age one year, and including the remaining 30%, the CA rate increased from 433 per 10,000 live births at age one year to 621 per 10,000 live births aged 0 to 5 years, a percentage increase of 43%. Restricting CA case ascertainment to age one year therefore effectively imposes a misleading cut off point for CA prevalence calculations. This cut off limits the generalizability of national CA prevalence estimates, especially in terms of service provision, developing models of care, and interventions for children diagnosed with CA at any age. This is because the support a newborn baby requires is different to that required for a three-year-old, for example.

Accurate prevalence estimates are essential for informing service provision (Law and Pascoe 2013). Study 1 has discovered not only an increase in prevalence of CA in Bradford, but that children often have more than one CA diagnosed at the same time. There are reports in the literature that the parents of children with complex conditions and comorbidities have reported experiencing duplications of services and inefficiencies, which have caused a significant impact on the whole family (Zhong et al. 2015). Comorbidities and co-occurring CA are also known to cause delays in essential early screening processes (Chapman et al. 2011), which place further demands on subsequent healthcare (Lindower et al. 1999; Colvin and Bower 2009; Grosse et al. 2009; Valderas et al. 2009; Chapman et al. 2011; Diederichs et al. 2011; Fitzsimons et al. 2013; Polita et al. 2013; Zhong et al. 2015; The Kings Fund 2016; Shetty et al. 2016). Although not all CA require long-term treatment, as some structural CA can be corrected with surgical procedures,

early detection is important for ensuring as many children with CA as possible can receive appropriate treatment with corrective procedures, as well as the rapid implementation of treatment plans for long-term CA such as thalassemia, and sickle cell disorders. Both of these steps help reduce the need for crisis management at a later date (WHO 2016).

Reducing costs and time spent ascertaining disease prevalence using feasible methods such as those of study 1, which do not demand the time of NHS consultants, are also vital for preventative care. According to the Office for National Statistics (ONS 2015b), spending in the whole of the UK on preventative care increased by 5.6% from £9.1 billion in 2014, to £9.6 billion in 2015, which accounted for costs of care designed to both avoid diseases (primary prevention) and the early detection of disease (secondary prevention).

5.2.2 CA case ascertainment by bodily system group

There are further similarities in the profile of CA disorders in study 1 to those of previous CA studies which helps further validate findings. The profile of CA in terms of bodily system group was found to be largely consistent with those reported previously (Devine et al. 2008; Greenlees and Garne 2009; BINOCAR 2014; Sheridan et al. 2013; Sokal et al. 2013; EUROCAT 2012). The only exception was nervous system disorders, seen as the most common group of CA in study 1, and in other CA research specific to the UK (Sheridan et al. 2013; BINOCAR 2014). For example, when including only CA diagnoses ages 0 to 1 years in study 1, and excluding metabolic and chromosomal disorders, the bodily system groups with the highest prevalence were CA of the nervous system, circulatory system, urinary and limb respectively.

When adding children aged 0 to 5 years and repeating the prevalence calculations study 1 finds the ordering of CA by bodily system group stays the same, but more children with a CA of the circulatory system were found

(Table 2) compared to those reported in the same cohort of children in phase 1 (Sheridan et al. 2013), and those reported in BINOCAR (2014). Again, an increase in the number of heart CA diagnosed post age one year is similar to other studies using primary care data for CA case ascertainment. One study comparing the prevalence of circulatory system CA in children aged 0 to 1 years to children aged 0 to 6 years, found the prevalence to be higher in children aged 0 to 6 years (Wurst et al. 2007b). Two studies using the CPRD primary care database found an increase in CA of the circulatory system, when including diagnoses made after age one year (Wurst et al. 2007b; Hammad et al. 2013).

A further study using THIN (2017) found a higher number of ventricular septal CA than those reported by EUROCAT (2013), and proposes this could be due to a large proportion of ventricular septal cases closing before the child reaches age one year. If this is true, the child is less likely to have their ventricular septal CA registered with EUROCAT (2013), but the diagnosis is recorded in primary care data (Wurst et al. 2007a), resulting in an underrepresentation of ventricular septal cases before the age of one based on EUROCAT (2013) data. This is further confirmed by primary care CA case ascertainment studies which find delayed diagnoses in around 10% of congenital heart defects (Wurst et al. 2007a), and a nearly 50% higher prevalence of heart CA than EUROCAT (2012) (Devine et al. 2008). Late detection of heart CA could also be attributable to some cases being missed at antenatal screening due to detection being difficult (Lee 2006).

Study 1 found a 210% increase in the number of skeletal dysplasia's diagnosed for children aged 0 to 5 years compared to children aged 0 to 1 years. This is a similar finding to another CA ascertainment study which also used primary care data (Sokal et al. 2015) and found marked increases in skeletal dysplasias when comparing those diagnosed at age five years and those diagnosed at age one year. Limb CA, specifically in hips, was found to be higher when compared to national CA rates in another primary care study (Sokal et al. 2013). It has been suggested this could be due to miss

classification between hip dislocation, classed as a major CA, or subluxation, classed as a minor CA (Shipman et al. 2006).

As well as the 210% increase in skeletal dysplasias, other significant increases in CA by bodily system group can be seen for nervous system CA (129%) and respiratory CA (44%). Looking at the CA diagnoses more closely in study 1, the increase in skeletal dysplasia's in the BiB cohort was due to a large number of children being diagnosed with short stature, which is considered to be a CA. The increase in nervous system CA was due to an inflation of congenital hearing loss in Bradford which is classed as a nervous system CA. Respiratory disorders are already known to be high in Bradford, which partly explains the increase in respiratory CA found in this study (Bradford Joint Strategic Needs Assessment 2014).

When including metabolic and chromosomal disorders in the CA prevalence calculations, there is a slight difference in the CA prevalence rates between study 1 and the national CA rate. Study 1 found the prevalence of metabolic and chromosomal disorders for children ages 0<1 to be lower than the prevalence reported by BINOCAR (2014). When including the additional CA cases in children diagnosed up to age five years, this difference is slightly less, but study 1 still reports a lower prevalence of metabolic and chromosomal disorders than that of BINOCAR (2014). Low reporting of metabolic and chromosomal disorders for children aged one year using primary care data has been found in another CA study, which argued that the complexity of metabolic and chromosomal disorders means their symptoms often take longer to assess and diagnose after birth (Devine et al. 2008). Although this may seem like a contradictory argument to the previous one to extend the age for case ascertainment to allow for increased CA diagnosis and prevalence, metabolic and chromosomal disorders may be an exception to this rule. A CA register may discover additional rare and complicated metabolic and chromosomal CA at an early age because they have close relationships with cytogenetic laboratories (Devine et al. 2008; Savva and Morris 2008). A study using the THIN primary care database to extract CA,

also found the prevalence of chromosomal CA to be lower, compared to those reported by EUROCAT (2013) (Sokal et al. 2013).

The findings from study 1, combined with the findings from previous primary care database studies adopting similar data extraction and CA coding methods to study 1, and finding similar patterns of CA prevalence when stratified by bodily system group to study 1 (Charlton et al. 2010; Sokal et al. 2013; Wurst et al. 2007a; Wurst et al. 2007b; Devine et al. 2008; Sokal et al. 2014; Hammad et al. 2013), help to confirm that it is possible that more than 2% of CA diagnoses are made after the child is one year old. These findings challenge the opinion of CA registers that state it is not necessary to collect CA after age one year (BINOCAR 2014). Some of the conditions in these subgroups are not expected to be detected in the prenatal period (Garne et al. 2011), but our data suggest that they may be taking longer to diagnose than previously thought, which has significant clinical implications. Delayed diagnoses are seen to create increased complications with care coordination and create a reliance on emergency care (Kim et al. 2006; Chapman et al. 2011; Ellison et al. 2013; Peterson et al. 2013). CA registers need to make improvements to their current methodologies for the detection of later CA diagnoses. A delayed CA diagnosis may not be solely due to poor case ascertainment by CA registers however, as the causes of childhood disability are further complicated by comorbidities and by social and genetic factors, making time to diagnosis a complex process that can differ between individuals with similar clinical presentations (DH 2012).

In England the recently established CA register NCARDS (PHE 2015) specifies that they do intend to collect data, including risk factors, via CA notifications after age one. The service however is new, and the longer term picture in terms of comprehensive ascertainment is not yet known. Study 1 demonstrates that CA case ascertainment is strengthened with the use of electronic primary care data. Consequently, CA registers which restrict case ascertainment up to age one (Greenlees and Garne 2009; BINOCAR 2014), may result in implications in terms of underestimating healthcare services for children with CA. There is also evidence to suggest late detection of complex

conditions such as CA are also associated with increases in healthcare use (Ellison et al. 2011; Petersen et al. 2013).

5.2.3 Maternal risk factors for CA

Study 1 also assessed the effect of updated CA ascertainment on the point estimates and statistical significance of the risk factors for CA reported in the phase 1 study (Sheridan et al. 2013). Drug use during pregnancy was also added as a risk factor which was made possible through linkage to primary care data. In phase 1 (Sheridan et al. 2013), the most significant risk factors were consanguinity to first-cousin level in mothers of Pakistani origin, and maternal age (>34) for white British mothers, as well as finding education to degree level protective. In study 1, there was no substantial change in the risk factors between the case ascertainment methods of phase 1 (Sheridan et al. 2013) and 2, even with a slightly different CA profile. This is an important finding as changes to the statistical significance of risk factors would have had implications for comparative analyses between CA registers with different ascertainment methods.

The results of the risk factor analyses in study 1 also show an excess risk to children born with CA to mothers in the least deprived IMD fifth overall, a finding also found in phase 1 (Sheridan et al. 2013). However, in both phase 1 (Sheridan et al. 2013) and phase 2, the numbers are very small so should be treated with caution (

Table 5). If the sample size of children with CA was larger in phase 1 and phase 2, deprivation may have had a larger affect as there is considerable evidence from the UK which recognises marked health inequalities between the least deprived and most deprived regions of the UK (Newton et al. 2015). Living in the most deprived communities in the UK is linked to a life expectancy of seven years less that the least deprived communities (The Marmot Review 2010). Furthermore, people living in Bradford have been reported as living 20 years less than people living in Surrey (ONS 2014). Considering the link between deprivation and increased health system

demand is essential when commissioning services for children with complex healthcare needs.

When including drug use during pregnancy to the maternal risk factor analysis, it was not found to be significant. This result is remains consistent with the literature exploring different drugs taken during pregnancy and the risk of CA. While some studies have indeed found a link between maternal drug use and CA (Patel and Burns 2013), overall the evidence is mixed. Antipsychotic prescriptions, one of the drugs included as a maternal risk factor in study 1, were not linked with CA at birth in two studies (Ban et al. 2014; Petersen et al. 2016b). However, when stratifying analyses to specific drugs, two studies discovered Paroxetine which is a type of anti-depressant, was associated with an increases in CA of the circulatory system (Reis et al. 2010; Ban et al. 2014). The association between anti-epilepsy drugs and an increased risk of CA was reported in a further three studies (Morrow et al. 2006; Tomson et al. 2011; Hernandez-Diaz et al. 2012). In study 1, drugs were not split by specific brands or types, which did not allow this detailed level of analysis. Also prescribed drugs which are recorded in primary care data, does not necessarily mean the drugs were taken, which may also have affected the results.

5.2.4 Limitations

Despite making several attempts to ensure CA extracted from primary care data was valid, the following limitations to this study have been identified. As confirmed by other primary care database studies, the date of diagnoses entered into primary care system has been reported as later, on average, than dates of diagnoses by GPs (Hammad et al. 2013). In study 1, according to local clinical experts, this is because CA diagnoses that are the result of consultant appointments are sent via letter to the GP practice, where the diagnosis codes are entered into the system. This means there may be a time lag on the date of actual diagnosis to the date entered into the GP

system, therefore time of diagnosis based on extraction from routine health data may need to be treated with caution.

There are ways to improve the validation of both exact diagnosis and date of diagnosis, by sending questionnaires to GPs requesting confirmation of diagnosis and date, or using medical records to determine the original consultant appointment and corresponding diagnosis. One study using medical records to confirm 188 CA diagnoses from 16 years of retrospective primary care data, found an 85% agreement between the CPRD and medical records (Charlson et al. 2010). A study investigating the prevalence of neural tube CA in the CPRD found 232 cases, and sent questionnaires to each cases GP to validate the diagnosis. One hundred and sixty-five (76%) GPs returned these questionnaires, which confirmed 71% of the neural tube CA diagnoses (Devine et al. 2008). A further study using the CPRD to ascertain heart CA contacted GPs to confirm 888 heart CA diagnoses. GPs returned 719 (81%) questionnaires which validated diagnoses for 93% of heart CA identified in the primary care system. This same study also found that 31% of heart CA diagnosed in the primary care database had a different date recorded electronically than the date confirmed by the GPs using questionnaires. Ten per cent of the date of diagnoses fluctuations found in this study were within 30 days of the date identified in the GP database (Devine et al. 2008). A final study using the CPRD to identify heart CA using seven years of data, found 484 heart CA diagnoses, 95% of which were confirmed by questionnaires sent to GPs.

Reading through free text information available in the electronic record, and sending questionnaires to GPs, although a useful validation method is also very time consuming. Study 1 reached 83% agreement using a clinician review approach of the CA diagnoses found, and 100% agreement when comparing the CA diagnoses found to a sample of each CA cases complete GP record (Section 3.4.5). Furthermore, the literature reporting similar validation methods for CA case ascertainment using primary care data collectively reached around 80% agreement, similar to the 83% agreement found in study 1. For more complex cases, or if two codes for the same

disease appear in the same record, then the full GP record should be requested and the free text information reviewed (Wurst et al. 2007b).

It was also discovered during the validation of clinical coding between phase 1 (Sheridan et al. 2013) and 2, that some CA did not match, and it was later discovered that some of these children had changed GP practice a few times. Evidence from other CA studies suggests that the patients in the GP system who do not move GP practice, may end up with slightly higher accuracy of diagnoses in their GP records and greater accuracy of diagnosis dates. It is worth considering when repeating CA case ascertainment studies using primary care data, that the flagging of cases found in GP records that have remained at the same practice will help identify those likely to be lower risk of bias, and those who have transferred GP practice many times, to be higher risk of bias (Hammad et al. 2013).

Cross-mapping of CTV3 to ICD-10 (WHO 2010b) is also vulnerable to discrepancies due to multiple CTV3 codes matching one ICD-10 code (WHO 2010b). Potential discrepancies were accounted for by performing a clinical review to assign the most appropriate CTV3 code to ICD-10 (WHO 2010b) match. A strength of phase 1 (Sheridan et al. 2013) was it did not require this step as medical diagnoses were extracted directly from medical records and converted to ICD-10 codes (WHO 2010b). However, despite this it was discovered that phase 1 (Sheridan et al. 2013) had coded some medical diagnosis with ICD-10 codes (WHO 2010b) that were not in the recommended list for inclusion as per EUROCAT (2013) guidelines. This means that some CA coded in phase 1 (Sheridan et al. 2013) will not have been in agreement with the CA extracted by CTV3 in phase 2, even though they may have been referring to the same conditions. This process highlighted one of the limitations of approaching data extraction using a CA codebook, as there are likely to be diseases that are perhaps rarer, that do not have equivalent ICD-10 codes (WHO 2010b) purely due to their novelty. The ideal solution would be to have the complete codebook reviewed by a clinician, and new diagnoses occurring added to the codebook. It was impossible within the time frame of this study to have the whole codebook

reviewed, which is why only those cases that were in disagreement between the primary care database and phase 1 (Sheridan et al. 2013) were reviewed by a clinician. This means the number of children that were included in both the phase 1 (Sheridan et al. 2013) and phase 2 data extraction are likely to be higher than the quoted 296 in this study.

A limitation of primary care data is that CA cases which are stillborn or diagnosed in the antenatal period that result in termination, are not well recorded in women's primary care records. One CA study found foetuses diagnosed with a major CA had a high likelihood of termination of pregnancy, at 50% for consanguineous unions, and 60.9% for non-consanguineous pregnancies (Becker et al. 2015). BiB does not report terminations of pregnancy or miscarriages because recruitment is at 26–28 weeks' gestation.

5.2.5 Conclusion study 1

Study 1 combined the personal and clinical information from the BiB cohort study with routine primary care data to produce a more comprehensive assessment of the impact of CA in children. This study adds to the growing area of research around the use of primary care databases for identifying CA cases in children. The study demonstrates more complete case ascertainment of CA can be achieved through linking cohort study data to primary care data making it possible to detect later CA diagnoses up to the age of five years. Thirty per cent of CA cases were identified after age one, suggesting that CA registers may need to reconsider their methods of case ascertainment and incorporate routine health data rather than relying on CA notifications. Study 1 also finds magnitudes of association for maternal risk factors for CA remain the same after increasing the sample size of CA, further validating primary care ascertained CA diagnoses. The increased prevalence of children living with CA in the community may require additional specialist resources for paediatric, obstetric, and genetic care for this, as-yet,

under-ascertained cohort. The results could also have implications for transition to adult services.

5.3 Key findings from study 2

Study 2 used the population of children with CA ascertained from study 1, linked to data from primary care records, use of hospital services, referral information recorded in each child's medical records, and the detailed maternal clinical, social and environmental information from a large ongoing birth cohort study. The aim of which was to examine how healthcare is delivered for children with CA, as an exemplar for children with complex healthcare needs, who have varying healthcare needs which are not well understood. The influence of factors aside from the child's ill health, such as deprivation and ethnicity on healthcare use were also addressed. The following key findings were identified:

1. Primary care consultations, use of hospital services and referrals to specialists were higher for children with CA than children without CA.
2. Children of Pakistani origin consulted primary care 50% more (multivariate IRR, 1.50, 95% CI 1.44 to 1.56) than white British children.
3. Children from economically deprived neighbourhoods were more likely to be admitted to hospital (multivariate IRR, 1.41, 95% CI 1.31 to 1.52) than consult primary care (multivariable IRR, 1.01, 95% CI 0.98 to 1.04), whether they had a CA or not.
4. Children with CA had a higher use of hospital services (multivariate IRR, 4.38, 95% CI 3.90 to 4.92) than primary care consultations (multivariate IRR, 1.27, 95% CI 1.20 to 1.35).
5. Children with higher educated mothers were less likely to consult hospital services (multivariable IRR, 0.84, 95% CI 0.75 to 0.94).

6. After controlling for the child's ill health, healthcare use for children with CA reduces but still remains at an increase, suggesting other factors are affecting the demand for healthcare, not solely ill health.

5.3.1 Describing healthcare use for children in the BiB cohort

One of the ultimate challenges for healthcare systems is to deliver healthcare services in concordance with the needs of individuals (Forrest et al. 2009). In order to plan and deliver healthcare services effectively, those responsible, such as commissioners, policy makers and providers, require information about the service needs of the local population and the current healthcare capacity to meet those needs (Turner-Stokes et al. 2013). The combination of hospital, primary care and audit data, to improve quality as well as identifying patients who most need health and social care, is an aim of the NHS Five Year Forward Review (NHS England 2014). The National Audit Office recommends NHS England still needs to improve the data it collects on demand and supply of healthcare services for the whole UK population (The Kings Fund 2016a). To understand the interchangeable healthcare needs of children with CA, the literature review (chapter 2) helped guide the choice of data sources in study 2.

The literature suggested a combination of primary care consultations, use of hospital services and referrals to specialists was required to comprehensively investigate health service use for children with CA (Dawson et al. 2013; Pasquali et al. 2013; Crooks et al. 2015), but had not been thoroughly addressed before using data linkage studies. Most of the literature that had previously investigated healthcare use for children with CA, came from American studies looking at hospital use for the treatment of heart CA specifically (Peterson et al. 2013; Dawson et al. 2013; Pasquali et al. 2014; Simeone et al. 2014; Agarwal et al. 2003), with very few studies addressing the demand on primary care services for children with CA (Billett et al. 2008; Wood and Wilson 2012). Using a combination of routine health data sources was important to help depict the severity of different CA, as well

as overall health service use. Primary care data, although able to capture larger proportions of patients with multi-morbidity, does not capture diseases of greater severity, which are more likely to be treated in secondary care. This means the number of primary care consultations does not independently predict severity of a condition (Crooks et al. 2015). This process of combining data sources to extract different elements of a child's healthcare needs, such as function, severity of condition, and definitive diagnoses, was illustrated in Figure 4 of Chapter 3.

Study 2 attempts to address this gap in the literature and in doing so, discovers that children with CA have higher numbers of primary care consultations, use more hospital services, and are referred to multidisciplinary specialists more often on average per year than children without CA. While this finding may not be surprising, it is important that it is quantified, as it provides the longitudinal data which evidences the healthcare needs of children with CA requested by the Chief Medical Officer (2013b). Using information such as the findings from study 2 to understand a child's healthcare needs in depth is the first step towards improving care for children with complex healthcare needs. It is when this in depth understanding is achieved that services can be best designed, sufficient and appropriate healthcare staff can be trained and all families can be supported (Fonseca et al. 2014; Narramore 2008).

When interpreting some of the more nuanced findings from study 2, it helped illuminate that there were also contrasts in healthcare use dependent on each child's ethnicity. Considering the healthcare use for children in the BiB cohort stratified by ethnicity, children of Pakistani origin had almost double the number of hospital admissions, and 2.4 more primary care consultations per year than children of white British origin. In the statistical analyses, children of Pakistani origin and other ethnicities were predicted to require more primary care consultations. This might be explained by more than half (53%) of children with CA in the BiB cohort being of Pakistani origin, but in other research using primary care linked BiB cohort data, mothers of Pakistani origin were found to also use primary care more than white British

mothers (Kelly et al. 2016b). It is not unreasonable to draw similarities between healthcare use for mothers and children in the BiB cohort, due to children's dependence on their parents for accessing health services (Forrest et al. 2009).

Children from economically deprived neighbourhoods had an increased use of hospital services, but not an increased use of primary care consultations. This finding is similar to previous research. Firstly, this might be explained by previous findings from the BiB cohort, which suggests mothers from poorer backgrounds are less likely to use primary care services due to variation in primary care practice provision (Kelly et al. 2016b). Secondly, neighbourhood level poverty has previously been associated with lower rates of primary care use (Dies Roux and Mair 2010, Larson and Halfon 2010). Positive outcomes for children therefore are predicted to be associated with higher use of primary care services as a preventative strategy, and less emergency hospitalisations (Starfield et al. 2005, Adler and Rehkopf 2008). Other evidence suggests patients that are in need the most are also often the most hard to reach (Waltenberg 2010; Rahman 2014). Children living in poor neighbourhoods, with parents who are recent migrants or those with low parental education are known to be at high risk of poor health and less optimal use of healthcare (Rosenkotter et al. 2012, Sado et al. 2014, Serbin et al. 2014). It is likely the high level of deprivation in Bradford has a direct effect on the rate of child deaths (CDOP 2016), which may be reflecting the number of admissions for children with CA. Patients in the most socioeconomically deprived groups experience long-term conditions and multi-morbidity much earlier in life than those in less deprived areas (Barnett et al. 2012). Also people with multi-morbidity are likely to be clustered in areas that are most deprived, which is likely to further exacerbate poor health (The Kings Fund 2016b).

There was only one factor which was associated with a reduction in the amount of healthcare use. Maternal age (>34) was associated with a lower use of hospital services. One explanation for this finding could be similar to that of other research which found that premature infants born to adolescent

mothers have been found to have significantly higher rates of hospitalisation and emergency admissions compared to premature babies born to older mothers (Ray et al. 2010). Furthermore, after controlling for ill health in the analyses, this reduction in the use of hospital services did not change significantly for older mothers, which means that the ill health of the child was not affecting healthcare use and was more likely to be external factors. Children born into consanguineous families were predicted to have an increase in the use of hospital services, but not primary care consultations. This finding may be linked to the results of study 1, which found that more children born as a result of consanguineous unions, had a CA, thus are more likely to have significant healthcare needs.

5.3.2 Describing healthcare use for children with CA

When stratifying the analysis by CA, children with CA were predicted to require an increase in primary care consultations and hospital services compared to children without a CA, although the increase in use of hospital services was predicted to be higher than the demand for primary care consultations. Addressing inappropriate admissions is a key priority for action to reduce heath inequalities in the NHS (NHS England 2016c), therefore understanding the impact children with CA have on the use of hospital services is essential to help healthcare decision makers allocate funding to areas where admissions are higher. Only one study was found which reported an increase in primary care consultations for children with CA, but for children with heart CA specifically (Billett et al. 2008). When adjusting for ill health the increased use of hospital services reduces by almost half, suggesting the child's ill health is in part responsible for the use of hospital services. Increases in the use of hospital services for children with CA are frequently reported in the literature (Billett et al. 2008; Colvin and Bower 2009; Dawson et al. 2013; Soneda et al. 2012; Polita et al. 2013; Agarwal et al. 2016; Cedars et al. 2016; Islam et al. 2016), however study 2 also finds the type of hospital admission differs between children with and without a CA.

Differences in the type of hospital admission in study 2 are most likely explained by CA requiring more complex treatment than those for children without CA. For example, although respiratory conditions were the most common reason for use of hospital services for both children with and without CA, a similar finding to other studies (Colvin and Bower 2009; Agarwal et al. 2016; Soneda et al. 2012), other emergency admissions were the most frequently used hospital service for children with CA. Other emergency refers to procedures of urgency requiring corrective and sometimes surgical interventions that are initiated by health professionals, rather than parents presenting with their child at accident & emergency. This increase in other emergency and elective procedures for children with CA has been found in previous studies (Polita et al. 2013).

Demand in healthcare services including hospital admissions stratified by type and reasons for admission are key when aiming to understand the healthcare use of a population, to ensure funding meets demand. Organisations such as the HSCIC (2015), which reports yearly evaluations of the number of hospital episodes in the UK, report increases in emergency admissions to hospital due to an aging population, and does not mention the demand on healthcare services due to children with complex healthcare needs. The increase in hospital services for children with CA seen in this thesis, which analyses just a small sample of all children in the UK, begs the question as to whether HSCIC (2015) data accurately reflects admissions for children with complex healthcare needs and more specific analyses are required to uncover areas where the impact lies. This could be an example of how poor ascertainment of childhood diseases due to the methodological deficiencies of national disease registers such as those identified in study 1, are leading to underestimations of healthcare use. Data on the use of hospital services a child with CA receives, is not only valuable for commissioning services, but for feedback to parents and carers to help lower their anxieties about the expected level of care for their child (Fitzsimons et al. 2013). Given the findings from study 1, that many CA are diagnosed later in childhood and are under ascertained due to the methodological constrains

of national registers (Greenlees and Garne 2009; BINOCAR 2014), results in the healthcare use for late diagnoses could also be underestimated.

In the analysis of referrals to specialists, 194/200 (97%) children with CA had at least one referral to a specialist. It was more common for children with CA to have two referrals to a specialist (42/200, 21%) than one (20/200, 10%). In the regression analyses children with CA also had an increased risk of referrals to specialists compared to children without CA, after adjusting for confounders. Although patient complexity increases the need for healthcare (The Kings Fund 2016a), coordination of appointments for the multiple specialists required is also susceptible to variation, and is sometimes exacerbated by the divide between primary care, community and hospital services (Department of Health 2013b). Divisions between services that provide care for one child is also associated with patient complications, late diagnosis and an increased reliance on emergency care (Kim et al. 2006; Chapman et al. 2011; Ellison et al. 2011; Peterson et al. 2013). A reliance on emergency care rather than preventative solutions offered at primary care level, leads to avoidable increases in costs (Petersen et al. 2013; Mavroudis et al. 2015; Rare Diseases UK 2015; Luthy et al. 2016; Genetic Alliance UK 2016).

The large increased risk of referrals to specialists for children with CA, but also the overall diversity in services accessed emphasises the complexity of their needs, and the complex healthcare management they need (Hunter 2014). Prospective data such as that of the BiB cohort study and longitudinal routine health data, has the ability to evidence childhood healthcare use, in the context of the challenging prognoses of children with complex healthcare needs and multiple comorbidities (Colvin and Bower 2009; Grosse et al. 2009; Diederichs et al. 2011; Polita et al. 2013; Zhong et al. 2015; The Kings Fund 2016b; Shetty et al. 2016). These complexities pose challenges in terms of coordinating multiple specialists, and although the results of study 2 do not provide information on how to better manage children with multiple comorbidities, the data is there to evidence that these children exist, and require input from a range of specialists. Services which require the most

additional resources are highlighted. Referring back to one of the key themes for ensuring the health system is prepared for children with complex healthcare needs mentioned in chapter 2; complexity might be best managed by increasing the efficiency of care coordination using key workers. Key workers help patients with complex needs navigate their way through different healthcare services and reduce duplication of care (Garland et al. 2001; Law et al. 2011; DH 2013b).

There was an identified underrepresentation of the services provided by some healthcare professionals in the medical records. Occupational therapy, genetic counselling and physiotherapy for example, were particularly underrepresented. This was surprising given the high levels of functional needs children with CA present with, needs which can be supported by occupational therapists and physiotherapists who provide specialist equipment and functional assessments (NHS England 2017a). Similarly, the support provided by genetic counselling to families whose child is affected by a genetic CA (NHS Choices 2016), were also envisaged to be in high demand, but this was not seen. According to local clinical experts, who formed an advisory role throughout this thesis, genetic counselling is only available following genetic diagnosis. Not all children with CA are classed as having a genetic diagnosis therefore they are not eligible for this service. Local clinical experts suggest professionals such as community nurses, physical therapists and support staff all play a role in supporting families, but again this is not clear, and as a result data availability on the time invested by these services will be difficult to track. Occupational therapists, physiotherapists and genetic councillors are also known to have no targets for waiting times (The Kings Fund 2016a), which begs the question as to whether the demand for their services are accurately represented at all using both routine health data and referral information from paper medical records.

There is also evidence which suggests primary care practitioners experience feelings of uncertainty when managing children with complex conditions. This can lead to delays in decision making or hesitance to make referrals to appropriate specialists, consequently causing delays to patient care and

incurring high costs for the health service (Molloy and O'Hare 2003; Cooley 1999; Starfield et al. 2002; Grosse et al. 2009; Shnorhavorian et al. 2012; Rinke et al. 2013; Mavroudis et al. 2015). Poor communication and a lack of training regarding specialist referral routes for children with complex healthcare needs have also been associated with delays to referrals from primary care to secondary healthcare services (Cooley 1999; Rinke et al. 2013). There are however, good practice examples of educational programmes and toolkits which have been implemented in primary care, to promote early detection and appropriateness of referrals, build stronger links between primary and secondary care, and improve coordination and health outcomes for children with CA (Rinke et al. 2016; Petersen et al. 2013; Kim et al. 2006; Luthy et al. 2016). Integrated primary and secondary care is a key recommendation of the NHS Five Year Forward Review (NHS England 2014).

Adjustments for ill health were added to the statistical analyses for the healthcare services with the highest predicted usage for children with CA. These were hospital services and referrals to specialists. After controlling for ill health, the predicted increase in the use of hospital services reduces by almost half but still remains as does the predicted increase in referrals to specialists. This suggests that higher healthcare use may not be completely attributable to ill health, but could be affected by other factors such as deprivation, social problems, ethnicity and the characteristics of the primary care practice (Fortin et al. 2012; Smith et al. 2013; Kelly et al. 2016b). The workload crisis in UK primary care practices was revealed in a detailed analysis of primary care data by The Kings Fund (2016b). This investigation discovered that one of the principal causes of pressure on primary care practice was workloads becoming more complex, due to more patients with complex conditions. A second cause of pressure was diversity and deprivation (The Kings Fund 2016b), which is not always reflected by funding. This potential anomaly has been explored as examples of the inverse care law where those with the greatest need receive the least services (Hart 1971). This emphasises the importance of measuring both multi-morbidity and socio-demographic factors in combination with the

disease determined to be driving healthcare use (Fortin et al. 2012; Smith et al. 2013).

Another reason why children may access healthcare services for reasons other than ill health could be due to parenting styles. The healthcare use of a child with complex healthcare needs sometimes reflect the choices of the child's main carers and parenting approaches have been linked to the rates of healthcare uptake for the children (Rosenkotter et al. 2012; Sado et al. 2014; Malhotra et al. 2014; Serbin et al. 2014). High rates of health service use may be unrelated to the child's illness, and instead reflect parenting styles (Goldfeld et al. 2003). Parenting styles are known to influence various aspects of illness management and the type of health-promoting behaviour undertaken, both factors affecting their children's health outcomes (Serbin 2014, Janicke et al. 2001). Parental depression, anxiety and poor emotional health have been linked to lowered access to children's preventative care and increases in the use of emergency care (Olfson et al. 2003; Flynn et al. 2004; Minkovitz et al. 2005; Chee et al. 2008; Sills et al. 2007; Farr 2015; Serbin et al. 2014).

5.3.3 Limitations

Using a subset of diseases (CA) does not mean all children with conditions that may be complex are covered in this analysis. But in order to extract a population that was representative of complexity, and prevalent enough to create sample size groups large enough for comparison, CA were chosen based on the knowledge that they were high in numbers in Bradford, and known to require complex care (Sheridan et al. 2013). The healthcare use analysis was also based on the Bradford population, which might be interpreted as a limitation in terms of its generalizability. However, the results are applicable to other populations or NHS trusts across the UK, that also serve highly deprived and ethnically diverse groups of patients, characteristics known to be associated with CA (Sheridan et al. 2013).

A further limitation is the small exploratory sample size of 400 children for the multidisciplinary referrals analysis. It was not possible within the time frame of this study to request access to a larger sample of medical records. The use of paper medical records for capturing referral activity is also susceptible to missed information due to fluctuations in consultant record keeping, interpreting handwritten entries and missing records. This finding also helps illustrate the potential advantages of a 'paperless' record keeping ethos in healthcare services, and the future emphasis for ensuring the exchange of data between IT systems in all clinical settings. This will strengthen the interpretability of key information at the point of care for patients with complex healthcare needs (NHS Digital 2017b). Despite these limitations, an increase in referrals to specialists for children with CA was identified. Exploring multidisciplinary referrals was an epidemiologically relevant addition to the healthcare use analysis, as patients requiring NHS services with multiple conditions are now the norm rather than the exception (Boeckxstaens et al. 2015). Multi-morbidities incur additional costs and challenges to the healthcare service and therefore require constant evaluation by public health service initiatives (Diederichs et al. 2011).

When developing the measure of underlying ill health for adjustment in the statistical analysis, a count of CA and unique prescriptions were used. This could have been made more robust through the inclusion of health conditions that are not CA, in order to be more representative of general ill health. However, the ethics application for this study did not expand beyond children with CA. The count of unique prescriptions did include all prescriptions for any health condition and therefore this does represent general health well. Medication records can provide a more complete list of actively treated conditions than coded diagnoses because chronic conditions frequently require repeat prescriptions (Crooks et al. 2015). Counts of diseases and the number of drugs prescribed have also been used to measure ill health and disease severity in primary care settings (Valderas et al. 2009; Huntley et al. 2012). A combination of all diagnoses for each child whether they were a CA or not, may increase the efficiency of the ill health measure in the model and developing this is a question for future research.

Primary care data is likely to represent frequent attenders, who may have more complex medical conditions, which could increase prevalence of multi-morbidity observed at a particular practice (Fortin et al. 2012), and if counting all diagnoses for each child, CA or not in the ill health adjustment, over adjustment may occur. As frequent attenders of healthcare, may also acquire more diagnoses and prescriptions, it is difficult to differentiate between true ill health, or frequent attenders who are less ill. However, when measuring ill health using multi-morbidity measures, frequent attenders can only bias the when large groups of diagnostic categories are used, which is a different argument for including only CA in the adjustment for ill health measure (Brilleman et al. 2014).

Study 2 did not attempt to estimate the costs of healthcare use which for children with CA are known to be high (McCandless et al. 2004; Sheridan et al. 2013). Some research suggests that cost analysis may be misleading when simply counting the number of CA per child, as this method does not account for the possibility the effect of each CA are not additive. This means the cost of one patient with two different long-term conditions may not be more than the cost of two patients with one long-term condition each. It is argued by some authors however that allowing for the non-additive effect of multi-morbidity remains important given the proportion of children in the population with multiple conditions is quite high (Brilleman et al. 2013).

5.3.4 Conclusion study 2

This study quantifies healthcare use for children in the BiB cohort and children with CA separately, by combining primary care consultations, use of hospital services and referrals to specialists linked to detailed socio-demographic data from a longitudinal birth cohort. This analysis of healthcare use has revealed that hospital services are most in demand for children with CA, but also for children who were economically deprived whether they had a CA or not. The findings provide quantified evidence that the complex

nature of CA requires careful multidisciplinary management, which could be facilitated by strengthened coordination between primary and secondary care. The results of study 2 contribute to current research into healthcare use for children with complex healthcare needs, as it has been noted by some of the key drivers for equitable healthcare provision in the UK that longitudinal data is lacking which is able to evidence children's healthcare needs (DH 2013b). Additionally, most of the relevant literature quantifying healthcare use for children with CA is mainly in relation to congenital heart defects and hospital care based in the US.

5.4 Summary of key findings from study 1 and 2 combined

Both studies presented in this chapter are interlinked in many ways. To understand the healthcare pathways of children with complex healthcare needs, study 1 used children with CA for the study population. Based on supportive literature, linkage to primary care data not only increased the study population of children with CA, but allowed a validation exercise to take place which helped ensure the CA cases ascertained were valid, and strengthened the case for using primary care data for CA case ascertainment. Routine health data may also be more cost effective than collection of CA by national registers. Vital to the increase in the number of CA cases found was the use of prospective primary care data as the source for CA case ascertainment. This made it possible to extend the time period for data collection beyond age one year to age five years. Because of the additional cases of CA discovered using this approach, it is likely that services for the number of children with CA are underestimated. Study 2 takes the study population from study 1, and explores the impact of caring for children with CA and consequential complex healthcare needs have on the healthcare service. Central to doing so was the ability to perform data linkage between three sources of routine health data. These were primary care consultations, the use of hospital services, and referrals to specialists. The granularity of detail presented in study 1, in terms of stratifying the bodily

system categories of CA, and comparing their prevalence to those found in other CA studies, also contributes to the investigation of healthcare use. Understanding the types of complex conditions and in what quantity also helps prepare health systems for assessing impact. The addition of healthcare use data which helps identify services in highest demand and what other socio-demographic factors increase this demand, creates a composite evaluation of the health needs of the local population. These findings combined propose methods for firstly, ascertaining population of children with complex healthcare needs, and secondly understanding their demands on the healthcare system.

6 Recommendations for future research

6.1 Chapter overview

Chapter 5 discussed the key findings from studies 1 and 2 with a particular focus on their contribution to current knowledge in the field of CA case ascertainment and healthcare use of children with complex healthcare needs such as CA. In this chapter, the findings of this thesis in terms of their implications for shaping the delivery of healthcare for children with complex healthcare needs are discussed. The aim of doing so is to focus on the upstream aspects of health, organisations and policies, to promote information sharing between healthcare research and healthcare decision makers, and encourage evidenced-informed policy (WHO 2018). The epidemiological health needs assessment, mirrors this approach, and has been used as a frame of reference throughout this thesis, to ensure the data gathered has an end goal in mind that aims to understand the needs of a population, bring about change, and deliver healthcare services effectively (Williams and Wright 1998).

As with most new research findings that are constrained by time and resources, it is realistic to assume that there are some changes that can be made immediately based on the knowledge at hand, and some that require further research. The scoping review presented in chapter 2, concluded with the insight that in order to ensure health systems are prepared for managing children with complex healthcare needs, gathering quantitative evidence such as that of studies 1 and 2, to create a case for potential improvement, is only the first step. This evidence then needs to be used appropriately and strategically to help plan and commission healthcare services. Following this, ensuring relevant populations access the services they require is the next challenge. This chapter will therefore be structured as follows; Section 6.2 discusses which findings can contribute to evidence-informed policy in light of the findings from studies 1 and 2. Section 6.3 discusses how the evidence

from this thesis has formed the basis for further research, to plan and commission services appropriately. This chapter draws on some of the key themes identified for improving health system preparedness for children with complex healthcare needs in the scoping review of chapter 2. Search strategies were conducted to extract relevant literature and are included in Appendices 12-14.

6.2 What can be changed?

6.2.1 Using routine health data effectively to improve health systems

Failing to use information efficiently in healthcare can result in unnecessary levels of preventable ill health (HM Government 2014). This research provides an example of how evidence for change can be provided without huge injections of additional funding, through analysing routinely collected information about the health of local populations (The Kings Fund 2016a). Whilst clinical technology and medical devices have experienced revolutionary developments, the same cannot be said for data driven improvements to the delivery of health and social care (HM Government 2014). The lack of quantitative research evaluating current services is perhaps not surprising given the complexities of contact points for children with complex healthcare needs (DH 2012). It is imperative that more studies that mirror the approaches of this thesis and utilise existing healthcare data, are conducted to quantify the successes of individual services, and evidence the need to invest in service improvement.

Better use of data has the power to improve health, both transforming and reducing the costs of health and care services (HM Government 2014) and there are some data driven initiatives in children's healthcare. The National Maternal Health Intelligence Network (PHE 2015) aims to address gaps in services by making it possible to identify and select localities in the UK with poorer child outcomes, with a view to supporting transformations and

developments of children's services in those areas. For example, the average number of children in England dying before they reach one year old is 4.1 per 1,000 live births, but Bradford is above average at 5.9 deaths per 1,000 live births before the child reaches one year old (PHE 2015). Consequently, Bradford has measures in place to compensate for the high levels of child mortality, which includes a joint strategic needs assessment for children with complex healthcare needs. This needs assessment helps highlight the significant challenges local healthcare services are faced with, in order to provide healthcare that meet the demands of children with complex healthcare needs (Bradford Safeguarding Children Board 2016). While surveillance systems such as this provide some useful data, they do not provide the level of granularity presented in studies 1 and 2 which detail what kinds of, and how much, healthcare children with complex healthcare needs require to aid healthcare decision makers. A possible solution would be to link routine health data to national healthcare drivers such as the National Maternal Health Intelligence Network (PHE 2015), to improve the specificity of top down service improvements.

Primary care services are under increasing pressures, which could be eased by more appropriate use of data. The current pressures on primary care sometimes results in visiting a variety of different GPs within the same primary care practice, as well as fluctuations in the consultants seen in outpatient clinics. Although continuity of GPs is not always possible in primary care, accurate, streamlined and regularly updated patient information is vital for ensuring that, at the very least, a patient who receives consultations from different GPs is greeted with accurate, updated information about their health. Furthermore, sometimes GPs are burdened by large quantities of administrative duties, which can reduce their face to face time with patients. Increasing the detail of multidisciplinary information for patients on the GP system, can reduce duplication of services, and enable more streamlined coordination, allowing clinicians to focus on delivering the best care to their patient rather than being embedded in administration (HM Government 2014). Better sharing of patient data may therefore indirectly improve continuity of care from GPs. Continuity is not

only something patients prefer, but is also a motivating factor for teams, leading to better patient care (Addicott and Ham 2014).

There are some frustrating organisational barriers to repeating studies using routine health data. One of the biggest challenges facing healthcare commissioners is reducing inconsistencies in primary care data management systems used across the NHS (The Kings Fund 2016b). Patients and clinicians may not be aware of the problems this causes until patients require outpatient appointments or services out of area. Information can be inaccessible, lost or not recorded at all (HSCIC 2011). Complications of this kind were experienced in study 2 of this thesis, when attempting to capture referral information to outpatient appointments, which was not recorded electronically. Although modification of the data extraction process in study 2 allowed referral information to be captured from paper medical records, this would not be feasible on a larger scale. Data capture in the NHS should therefore be standardised across all trusts and practices with one information system used. A shift towards paperless record keeping for all health professionals is required. Secondly, more advanced technology for understanding free text information in medical records is promised by NHS England and should improve the reliability of outpatient data as well as patient record quality overall (NHS England 2016a). The development of natural language processing, which is a method for converting written information in medical records into data, has the potential to further help to validate diagnoses, removing the need for manually searching through paper medical records, and enabling a story to be told about each patient's journey (Lacy et al. 2017).

Another organisational barrier linked to the choice of primary care data management systems, is the extraction of diagnoses data coded in CTV3, requiring conversion to ICD-10 (WHO 2010b). This conversion process is necessary as most healthcare data and disease classifications (including HES) are organised using ICD-10 (WHO 2010b), thus enabling generalizability to other national and international studies. This conversion process is both error prone and time consuming. However, NHS Digital

(2017b) aims to introduce a Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT; NHS Digital 2017b), which uses a structured clinical vocabulary for electronic health records, and is currently the most comprehensive and precise clinical health terminology system in the world. The SNOMED CT (NHS Digital 2017b) vocabulary is also international, which will allow the UK to take part in more effective research and analysis of health information and support national and global health care improvements. Implementation of SNOMED CT (NHS Digital 2017b) into all primary care practices is aimed to be completed by 2018 (HSCIC 2013; NHS Digital 2017b), as well as introducing automated functions to further reduce the administrative burden on GPs (NHS England 2014). This will also reduce the amount of error when extracting data for prevalence studies from primary care. It is a further aim to give healthcare professionals real-time digital information on a person's health and care by 2020 for all NHS-funded services (HM Government 2014).

Appropriate use of data can also help to improve job satisfaction of GPs, and lead to better patient care. Increasingly primary care practitioners report feelings of impossible workloads, burnout and an inability to practice safely due to timed pressures (The Kings Fund 2016b). A recent survey commissioned by the Commonwealth Fund, identified 59% of GPs in the UK reported their job to be stressful (Osborn and Schneider 2015). The eighth national GP work life survey published in 2015, revealed GPs reported the lowest levels of job satisfaction since the introduction of their new contracts in 2004, and more GPs were quitting direct patient care than three years ago (Gibson et al. 2015). These levels of dissatisfaction have remained largely hidden until recently due to a lack of readily available primary care data (The Kings Fund 2016b). As well as coordinating care, routine health data also has the ability to identify specific primary care practices which are placed under more pressure than others. This can help to ensure resources match need, reduce pressures on GPs, and improve job satisfaction.

6.2.2 Improving coordination of care

The NHS Five Year Forward Review (NHS England 2014) identified three major areas for improvements to healthcare in the UK. These were the health and wellbeing gap, the care and quality gap, and the funding and efficiency gap. These gaps in services are noted to be made more complicated by the lack of integration between primary care, hospital care and services provided in patients' homes (NHS England 2014). In study 2, 21% of a sample of 200 children with CA, had more than one specialist involved in their care at any one time. Multidisciplinary clinics, disease specific centres or coordination led by primary care are among some of the suggestions for effectively managing the multiple services children with complex conditions require (Grosse et al. 2009). As identified in the scoping review presented in chapter 2, services which seem to excel in terms of coordination of care, involved close liaison with commissioning and management (Watson et al. 2002; Law et al. 2011; Bachmann et al. 2009; Pratt et al. 2012; Brooks et al. 2013), and contained clearly defined pathways which help support accurate referrals. Close liaison and clear pathways are also seen to help prevent over use of services which are already in high demand (Dale and Godsman 2000, Elias et al. 2012).

While the distribution of complex healthcare needs in different populations will fluctuate, as will availability of healthcare resources, a core model of practice that can be tailored to local needs is required, with strategies to improve coordination, communication and cooperation between both paediatric specialists and primary care. The Chief Medical Officer (DH 2013b) has frequently endorsed the role a key worker could play in coordinating and managing care for children with complex healthcare needs. The scoping review in chapter 2 also identified key workers as a catalyst for care coordination, but how a key worker might integrate into practice remained undecided in the literature and had not been subjected to significant evaluation (DH 2013b; Hillis et al. 2016).

While data sharing can help reduce gaps in services and provide the evidence for those that are placed under the greatest demand, key workers may provide 'on the ground' support for streamlining care. Shifting the healthcare culture away from a belief that a child's complex healthcare needs are the barrier to successful care coordination, towards holding the barriers to accessing services accountable, should be central to informing the key worker role (Looman et al. 2013; Farasat and Hewitt-Taylor 2007). Routine health data can be used to ensure the effectiveness of key workers. The Kings Fund (2016a) highlights the implementation of key workers should not only be supported by appropriate multidisciplinary staffing, but efficient and regularly reviewed analyses of primary care data, with the results communicated to the whole multidisciplinary team (The Kings Fund 2016a). Study 2 has demonstrated that patterns of healthcare use can be identified from routine health data to help prioritise areas for action for key workers.

Effective healthcare delivery relies on two key components, 'relationship continuity', defined as the continuous therapeutic relationship with a healthcare professional, and 'management continuity' which refers to consistencies in clinical management between the planning, coordination, handover, communication and information sharing phases of care (Freeman and Hughes 2010). Placing key workers responsible for managing children with complex healthcare needs within the primary care practice in which they work will improve relationship continuity. Allowing key workers to prioritise their workload and improve appropriate referrals using routine health data, improves management continuity. A combination of both relationship and management continuity will lead to the most effective management strategy for children with complex healthcare needs (Freeman and Hughes 2010).

Study 2 highlighted that children with complex healthcare needs require increased input from primary care and secondary care services albeit with secondary care being most in demand. This demand for hospital services in study 2, draws similarities with the pattern of healthcare spending in the UK, which was dominated by hospital services and inpatient care, totalling £41.1 billion worth of investment in 2015 (ONS 2015b). The answer to reducing the

burden on hospitals may lie in providing advice and support to manage conditions at home, linking with community teams. Multispecialty providers may assist in reducing the pressure on hospital services by providing enhanced urgent care services, but also education when the condition may not require urgent care (NHS England 2016a).

A very close second in terms of healthcare spending was outpatient care at £40 billion in 2015 (ONS 2015b). In study 2, children with CA were identified as requiring more referrals to specialists than children without CA, as well as having more than one specialist involved in their care at one time. Key workers are essential to ensure appropriateness of referrals to specialists in outpatient clinics as well as helping patients navigate the complexities of multiple service providers (Hillis et al. 2016). Integrated approaches supported by key workers, could also help improve appropriate referrals to outpatient care and improve cost efficiencies (DH 2011).

6.2.3 Multispecialty providers

Multispecialty providers are another proposed solution to coordination of care, and have been piloted in certain trusts, with the aim of relieving pressure on GPs. It is also their role to be care navigators, and prevent the automatic assumption that patients need to see their GP (NHS England 2016a). Multispecialty providers are a step up from a key worker, in that they are a team of healthcare professionals with a diverse set of skills, which can help coordinate care for the child as well as support families. Their roles are expected to involve both coordination of care, while simultaneously helping engage patients in treatment by performing home visits to those who miss consultant appointments (NHS England 2016a).

Rather than visiting the GP for a referral to a specialist, multispecialty providers can assess for and perform referrals thus reducing the workload of GPs. For example, this might include referring to an occupational therapist for specialist equipment, or arranging a visit from a community nurse. This

may further be facilitated by the introduction of smart phone applications, with portals providing information, symptom checkers and sign posting to other relevant services (NHS England 2016b). In Birmingham, which is a city with a similar ethnically diverse population to Bradford, and high infant mortality, schemes have been introduced which join together primary care, community based services and urgent care providers. These services are linked via a single point of contact, meaning multidisciplinary services can be accessed physically and virtually across three sites, seven days a week. Central to the success of multispecialty providers is the ability for GPs to access electronic patient records from all primary care practices. This means summaries of consultations provided at different services, will be sent to the patients registered practice (NHS England 2016b).

The multispecialty provider aims to integrate care, and dissolve the divide between primary, secondary and community services. They focus on designing care for the health of a population, irrespective of the local institutional arrangements that may be in place. It is this 'breaking down the barriers' approach combined with longitudinal statistics providing the evidence of the increase in healthcare use for children with complex healthcare needs that will make the most beneficial changes (NHS England 2016a).

6.2.4 Training healthcare staff

There are further ways to help maximise the clinical utility of centrally held datasets in primary and secondary care. These include ensuring outpatient appointments and referrals to specialists are coded in the GP system. Ensuring the quality of coded routine health data is the responsibility of all those who have contact with, prescribe or deliver healthcare to patients (NHS Digital 2017a; NHS Digital 2017b; NHS England 2016b). For clinicians, regular meetings with clinical coders within the same trust may help improve GPs and consultants recording of information into the GP system. Ensuring consistent data management systems also facilitates the development of

national standards and ensures data entry at its simplest form is consistent and comparable.

Primary care practitioners have reported feeling undereducated when managing rare and complex disorders in their patient caseloads, something that is exacerbated by a lack of training, time, and poor communication with specialist clinics (Starfield et al. 2002; Shnorhavorian et al. 2012). A lack of confidence can easily lead to inappropriate referrals to specialists, or worse no referral at all contributing to delays in care, and feelings of uncertainty and anxiety for patients as they are passed through services (The Kings Fund 2016b). More than 13 million referrals to hospitals for elective (planned) care in 2013 came from primary care, a number that continues to rise (PHE 2016), which adds magnitude to the potential consequences of inappropriate referrals. Multispecialty providers can improve communication between specialists using their contact with multiple professionals to bridge the gap between primary care practice and specialists in outpatient clinics (NHS England 2016a). In the absence of multispecialty providers, training tailored to local needs and delivered to primary care to strengthen communication links between GPs and specialist's receiving referrals are essential.

There are some good practice examples of educational programmes delivered in primary care, which intend to strengthen the links with genetic specialists, as well as providing specific training for complex genetic disorders. These training initiatives have shown promise for improving coordination and appropriate referrals for patients with complex genetic conditions that present at primary care (Kim et al. 2006; Luthy et al. 2016; Rinke et al. 2016; Gen-Equip 2017). Despite a few good practice examples, specialist training for managing children with complex healthcare for key professionals, parents and carers is in high demand (Fonseca et al. 2014; Narramore, 2008).

6.2.5 Ethnically diverse and deprived communities

When investigating the prevalence of children with complex healthcare needs and their associated healthcare use it is fundamental to consider geographical differences in prevalence, which may reflect patterns of deprivation (DH 2011). The evidence from study 1 in this thesis, and previous research, highlight the increased levels of CA in Pakistani communities and the increased numbers of Pakistani women living in deprived areas (Garner and Bhattacharyya 2011). Despite this, recent research into primary care practice provision, found less primary care practices, in areas that were most deprived and therefore most in need (Kelly et al. 2016b). This is an example of the inverse care law (Hart 1971), where service provision does not meet demand.

Multispecialty providers may also be able to help reduce inequalities in healthcare provision (NHS England 2016a). Instead of individual teams of professionals serving individual practices, multispecialty providers intend to join services together, providing services to populations that most require it. This might mean more than one primary care practice operating in the same locality, which has been identified as having higher levels of need (NHS England 2016a). It is the eventual aim of multispecialty providers to hold a single, whole population budget for the services they provide. This would contribute to tackling inequalities in health and disparities in care provision. A broader range of services in the community will be available, and for patients with very high needs and costs, such as children with CA living in deprived, multi-ethnic communities such as Bradford, ‘extensive care’ services will be available (NHS England 2016a). Analyses of routine health data will feed into the work of multispecialty providers and help shape the layout of these services to populations of people most in need.

6.3 What requires further research?

6.3.1 Increasing the generalisability of the research

One of the limitations of this research was the analysis of routine health data from one local population. There are ways to improve the generalizability of this research, and steps were taken throughout the methods used for CA case ascertainment and data linkage, to ensure these steps could be easily repeated using other routine health data across healthcare trusts. For example, there are other primary care databases used for healthcare research across the UK, which were summarised in chapter 2. Repeating the CA case ascertainment methods using other primary care databases would be one way of expanding the sample size of the study population once access to these databases were granted. Combining data sources to obtain more accurate prevalence estimates, especially when studying rare diseases, is a recognised method of increasing study populations (Coloma et al. 2010). There are also opportunities to link primary care data to other UK cohort studies to expand the analyses and tailor healthcare services to local needs. The UK Biobank for example is another primary care linked cohort study, which so far has successfully linked over 50% of 500,000 participants to primary care data in England, Wales and Scotland (UKBiobank 2016).

6.3.2 Identifying undiagnosed diseases

Populations of patients with undiagnosed conditions lead to challenges when trying to justify the need for appropriate healthcare services (Ramoni et al. 2017). The wide variety of rare and unknown conditions in Bradford (Sheridan et al. 2013), with differing age at onset, would exclude a large proportion of children for treatment if relying on a diagnosis for referral. This is why the choice of a definition of children with complex healthcare needs in chapter 2, had to identify the functional and psychosocial needs of children, rather than medical diagnoses (Baird, 2013). CA are increasingly complex conditions, difficult to diagnose, and sometimes so rare that an ICD-10 code

(WHO 2010b) does not exist to identify the condition. This problem resonated in the data collection methods of phase 1 (Sheridan et al. 2013), when clinicians identifying children with CA struggled to find an appropriate ICD-10 code (WHO 2010b), which caused problems identifying them in the primary care data during phase 2. Despite developments in rare disease research and new diagnoses being added to the ICD-10 (WHO 2010b), many patients remain undiagnosed for several years (DH 2013d; Howell et al. 2013; Prada et al. 2014; Shashi et al. 2013; Farwell et al. 2015; Rare Diseases UK 2015; Rump et al. 2016; Care4Rare 2017; Ramoni et al. 2017). Not surprisingly, the burden of undiagnosed conditions, whether they are CA or otherwise, are difficult to account for using routine health data, especially given the methods in this thesis base prevalence rates on confirmed diagnoses in primary care data.

Four in every ten patients in the UK report they find it difficult to receive a diagnosis (DH 2010). Symptoms and associated comorbidities make diagnosis increasingly challenging (DH 2013d). Studies from across the globe report lengthy wait times for receiving diagnoses that eventually turn out to be rare, genetic or complex in nature (Tifft and Adams 2014; Rare Diseases UK 2015; Ramoni et al. 2017; Care4Rare 2017; Howell et al. 2013). Overall the number of undiagnosed genetic disorders in a general clinical setting remains unknown (Shashi et al. 2013).

Missed diagnosis for CA or other complex conditions, which are less rare, but still remain life threatening if undiagnosed, is another public health problem that causes concern. However, this can be improved without additional genetic research and novel screening methods. There is a considerable body of evidence, briefly considered in study 1, which reports missed diagnoses of circulatory CA (Kuehl et al. 1999; Stochholm et al. 2006; Wren et al. 2008; Reich et al. 2008; Willis et al. 2009; Ewer 2013; Bartos et al. 2015; Kelle et al. 2015; Lannering et al. 2015; Mouledoux 2013). Although one of the most prevalent CA in new-borns (1 baby in every 1000), around 25% of children with circulatory CA remain undiagnosed (Wren et al. 2008; Mouledoux et al. 2013). In a study of 90 new-borns with circulatory CA,

nearly half were discharged home undiagnosed (Lannering et al. 2015). Ten per cent of children with serious undiagnosed heart CA are estimated to die before they have the chance to commence corrective surgery (Elsas et al. 1996; Ward et al. 1996; Ewer et al. 2013). The risk of heart CA presenting later in childhood includes avoidable health problems such as failure to thrive, sepsis or pulmonary hypertension (Ward et al. 1996; Middleton et al. 2014). Routine neonatal screening is often failing to identify heart CA (Kelle et al. 2015; Lannering et al. 2015), which is a significant public health problem (Reich et al. 2008). One of the findings from study 1, was that a large proportion of circulatory CA were detected using primary care data when increasing the age for CA case ascertainment from ages 0 to 1 to 0 to 5 years. The age for CA case ascertainment using primary care data has the potential to be further expanded, to identify patterns of missed diagnosis across different age groups, in order to learn from and improve detection of CA that are commonly missed.

Undiagnosed conditions, means the impact of children with complex healthcare needs on the healthcare service are underestimated. It is well documented that patients with undiagnosed condition are often subjected to multiple tests, specialist consultations and imaging studies in an attempt to find a diagnosis. Consequently, children with undiagnosed conditions can sometimes have more of an impact on the health service than children with a diagnosis (Need et al. 2012; Williams et al. 2014; Biesecker and Biesecker 2014; Farwell et al. 2015; Rare Diseases UK 2015; Romelczyk et al. 2015; Sawyer et al. 2016; Genetic Alliance UK 2016; Ramoni et al. 2017). Longer periods of time to diagnosis, combined with testing and genetic counselling, has been estimated at a cost per diagnosis of £20,050, excluding unplanned hospital admissions and clinic visits. The cumulative cost for repeat laboratory testing for undiagnosed conditions has been estimated at £942,862 compared to £558,615 for those who receive a diagnosis following testing (Shashi et al. 2013). A UK survey found 45% of 1,203 patients seeking a diagnosis saw more than 10 doctors before receiving a diagnosis (Rare Diseases UK 2015).

Using longitudinal analysis of routine health data to understand the healthcare use of children with complex conditions, which remain undiagnosed for a period of time, is also possible. Some researchers propose novel solutions for selecting risk factors for diseases from routine health data, before a diagnosis is made (Grosse et al. 2014; Yiallouros 2015). In particular, there are some risk factors that have been associated with underlying genetic conditions that have not yet been diagnosed, which once identified, can be the route to further investigations (Hosoki et al. 2009; Rapin et al. 2009; Herlihy et al. 2010; Okamoto et al. 2012; Howell et al. 2013; Visootsak et al. 2013; Biesecker et al. 2014; Fukami and Ogata 2014; Piton et al. 2014; Farwell et al. 2015; Lee et al. 2015; Terry et al. 2015; Wright et al. 2015). These risk factors may be the child's only diagnosis until further testing. The most common risk factors for suspected undiagnosed conditions are listed in

Table 11. Although an undiagnosed condition cannot be identified in primary care data, there are two ways in which routine health data can be used to help identify and contribute to the knowledge base for undiagnosed conditions. Firstly, finding ICD-10 codes (WHO 2010b) for risk factors where possible, to create an algorithm for extracting patients with potentially undiagnosed conditions from primary care data, which can then be subjected to further investigations. Secondly, those patients who eventually receive a diagnosis that was undiagnosed for a long period of time, can have their routine health data investigated retrospectively for patterns of healthcare use leading up to the diagnosis. This process could help identify risk factors, or patterns of service use, which could be linked with specific conditions. This means patients that display similar risk factors and patterns of service use can be identified for further testing or closer investigations.

Risk factors/ indicator	Supporting references
Delayed/ abnormal speech	Hunt et al. 2014; Fairbrother et al. 2015
Dysmorphic features	Rapin 2009; Okamoto et al. 2012; Biesecker et al. 2014; Hunt et al. 2014; Lee et al. 2015; Wright et al. 2015
Hypertonia / joint hypermobility	Visootsak et al. 2013; Hunt et al. 2014; Terry et al. 2015
Genital abnormalities	Herlihy et al. 2010; Fukami et al. 2014
Respiratory distress at birth	Hunt et al. 2014
Cardiac defects	Lee et al. 2015; Wright et al. 2015
Seizures	Howell et al. 2013; Farwell et al. 2015; Lee et al. 2015; Wright et al. 2015

Table 11: Risk factors for identifying undiagnosed conditions

Patterns of common risk factors and service use for patients who remained undiagnosed for long periods of time can also be used in training exercises for healthcare professionals. There are good practice examples outlining the utility of educational programmes to prevent underdiagnoses (Kim et al. 2006; Rinke et al. 2016; Luthy et al. 2016; Gen-Equip 2017). These have shown to improve both coordination of patients, increase efficiency and specificity of referrals, and increase primary care professional's confidence. Services that are key in the early detection of undiagnosed diseases need better links with rare genetic disease specialists to facilitate accurate referrals and diagnosis.

By the very nature of being undiagnosed, prevalence statistics for children seeking a diagnosis are difficult to ascertain. The use of routine health data serves an additional purpose in undiagnosed disease research, and would be an interesting springboard into further estimating the impact on the healthcare service of children with complex healthcare needs.

6.3.3 Understanding the distance travelled for care

Travel time and distance to services can also play an important role in healthcare use and management of care for children with complex healthcare needs (Delmelle et al. 2013). Children with complex healthcare needs who require more severe or specialist treatment are often referred to specialist centres for specific treatments. Although centralisation of specialist centres such as paediatric intensive care has many benefits including concentrating skills and expertise into a smaller number of high volume centres, it results in children having to travel further for specialist care. This also creates problems for timely access to care. A study investigating distance travelled for admission to paediatric intensive care units in the UK, found the median distance travelled in England was 21.8km in 2014 (Paediatric Intensive Care Audit Network 2014), and another paediatric study found travel time for treatment is generally greater than one hour (Cassell et al. 2013). A study looking at distance travelled for cancer treatment found 77% of patients do not actually live in the city where the principal treatment they need is available (Snelling and McDowell 2010). These figures seem more extreme when comparing them to the average distance travelled for routine healthcare. The distance travelled from a person's hospital to home is surprisingly short in most cases, with over half occurring within 6km (3.7 miles) (Roberts et al. 2014). Some evidence suggests that patients living further away from the healthcare services they need experience worse health outcomes (Kelly et al. 2016a). The association between distance travelled for care and health outcomes as well as indirect costs requires further research in terms of how this adds to the overall impact of children with complex healthcare needs.

6.3.4 Supporting families and carers

Parents not only have to become decision-making experts regarding the healthcare for their children, they also have to sometimes perform medical procedures, and deal with technical equipment. Because of this, reducing

caregiver stress is a critical step towards ensuring the best health outcomes for children (Goudie et al. 2014). Supporting parents and families was a key theme for improving health system preparedness for children with complex healthcare needs in chapter 2, but it was not possible within the scope and time period of this thesis to explore this area further. This is an interesting area for further research, as some authors have noted that high rates of health care use may not be solely related to a child's illness, but may also reflect parenting styles (Goldfeld et al. 2003; Horton et al. 2010; Yun et al. 2013). Further research into parenting styles may help understand disparities in parents or carers initiating access to healthcare for their child with complex healthcare needs (Prady et al. 2014). The links between parental stresses, levels of depression and self-esteem on parenting style, and how this directly affects uptake of healthcare requires further research (Horton et al. 2010).

Supportive parenting which involves having your child's best interests at heart but also being present, involved, encouraging and helpful, has also been associated with lower rates of nonemergency visits, which might suggest positive parenting approaches have a protective effect on health in early childhood (Malhotra et al. 2014; Serbin 2014). Patterns of parenting are seen to differ dependent on the social, economic and ethnic background of the family. Even in neighbourhoods with low socioeconomic status, which are often associated with high levels of emergency care visits, positive parenting behaviours are seen to moderate usual patterns of service use for disadvantaged families, resulting in lower rates of emergency visits, and higher rates of primary care use (Serbin et al. 2014). However, it has been noted that the association between positive parental behaviour's and frequency of consultations has not been intensively examined (Serbin et al. 2014).

Supporting parents and carers has shown positive results in some research, for example some studies have shown that it influenced the uptake of reproductive healthcare services (Bloom et al. 2001, Haque et al. 2012, Sado et al. 2014). An effective social network is regarded as a protective factor for parents as it increases mothers' self-esteem, provides a medium for sharing

experiences, and thus increases mothers' abilities to respond to their child's needs. Parents who experience better social support, report better parental coping with crises and improved accessing of healthcare (Gelkopf and Jabotaro 2013; Ercegovac et al. 2013).

Supporting parents could be partly addressed using longitudinal primary care data, as it is possible to monitor the care requirements of children with complex conditions, whose prognosis or care needs change as they develop (Cooley et al. 1999; Starfield et al. 2002; Crane et al. 2012; DH 2013a; Rinke et al. 2016). The data therefore allows each child's healthcare story to be tracked, and these stories can equip healthcare professionals with the knowledge required to prepare families and carers for their child's future care needs. Gathering in depth insights into the experience of caring for children with complex healthcare needs, will be best addressed using qualitative research, including semi-structured interviews with parents to understand parenting styles, and would be a valuable addendum to this research.

6.3.5 Patient and Public Involvement

The input of patients in research can help implement healthcare research and support decision makers. Patient and public involvement (PPI; NHS England 2017b) works on the premise that those who have experienced medical care are best placed to identify innovative and effective solutions (NHS England 2017b). Health and social care organisations now have a statutory duty to involve the public, and consult them in relation to their health and social care. Involving people is not always straightforward, and can take a considerable amount of time. When executed correctly however, involving patients provides opportunities to improve patient safety, patient experience and health outcomes. Excluding patients from decisions about their care can lead to poor practice (The Stationery Office 2013).

Planning how services will be delivered in terms of proposals for change, the way care is provided and any other decisions which might affect the

provision of care, needs to be addressed with a patient council (NHS England 2017b). One particular focus of PPI is ensuring access to care and inequalities experienced between socioeconomic groups are minimised (Marmot 2010). PPI prioritises capturing the needs of patients who experience the poorest health outcomes, in order to improve access to services, and reduce health inequalities (NHS England 2017b). Involving patients in healthcare commissioning helps healthcare provider's implement research, and also enables patients to learn about the services available to them as they become involved in the implementation process. The benefits of involving patients in research have shown impact at all stages, including the development of user focused research objectives, development of user relevant research questions and questionnaires and interview schedules (Brett et al. 2012). PPI would be particularly pertinent in future qualitative work addressing parenting styles, to ensure the interventions designed to support parents meet their needs. It is also important for healthcare decision makers to understand that people vary substantially in their preferences for participation in decision making. It should not be assumed that all patients want to take part in decision making, therefore patient preferences must be assessed individually (Levinson et al. 2005).

6.4 Conclusion

Study 1 of this thesis provided quantitative evidence of an increased prevalence of CA in a population of children with a wide-ranging disability profile and consequential complex healthcare needs. Study 2 highlighted which services were in highest demand for children with CA, and identifies factors which influence the use of healthcare services. Central to doing this study was data linkage between three sources of routine health data. These kinds of quantitative information have the potential to shape healthcare delivery, but its value remains unrealised until it is implemented within the context of current healthcare practice, and until it is supported by commissioners and key decision makers.

This discussion chapter has highlighted that there are some immediate organisational level improvements which can be made to healthcare services supporting children with complex healthcare needs, with the right backing from healthcare leaders. Efficient use of data has the power to make changes to healthcare organisations without huge injections of funding. Better use of data, working towards a completely paperless ethos and streamlining access to data between primary and secondary care will most likely see great improvements across the spectrum of healthcare. Learning from patterns of healthcare use can also form the basis for providing training to those providing care, pinpointing areas for action for multispecialty teams. This can help understand local needs and uptake of services dependent on the health determinants of the population such as levels of deprivation and ethnicity, and educating professionals on complex diseases that may go undiagnosed without additional testing and special attention.

The findings of this thesis could be further strengthened and made more widely applicable to healthcare practice through some important areas for further research. The most logical next steps include increasing the generalizability of the findings, by linking to other national primary care databases, ascertaining UK wide prevalence statistics for CA and potentially other complex conditions to determine whether risk factors differ in other populations. Using primary care data to identify risk factors that are commonly associated with undiagnosed conditions could help capture the healthcare use of children with complex healthcare needs who have not yet received a diagnosis. The impact children with complex healthcare needs have on the healthcare service could be further underestimated without understanding the distance children have to travel for care and the implications this has on theirs and their carer's health. Ensuring parents and carers are appropriately supported could be a solution to both reducing unnecessary visits to healthcare services while helping children receive appropriate care. Involving parents and carers in the design of services in the future is known to help boost the effectiveness of healthcare commissioning,

the delivery of services and contribute to tackling health and social wellbeing inequalities, and should be part of any change to future healthcare practice.

7 References

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8 Appendices

Appendix 1: Search strategy for scoping review

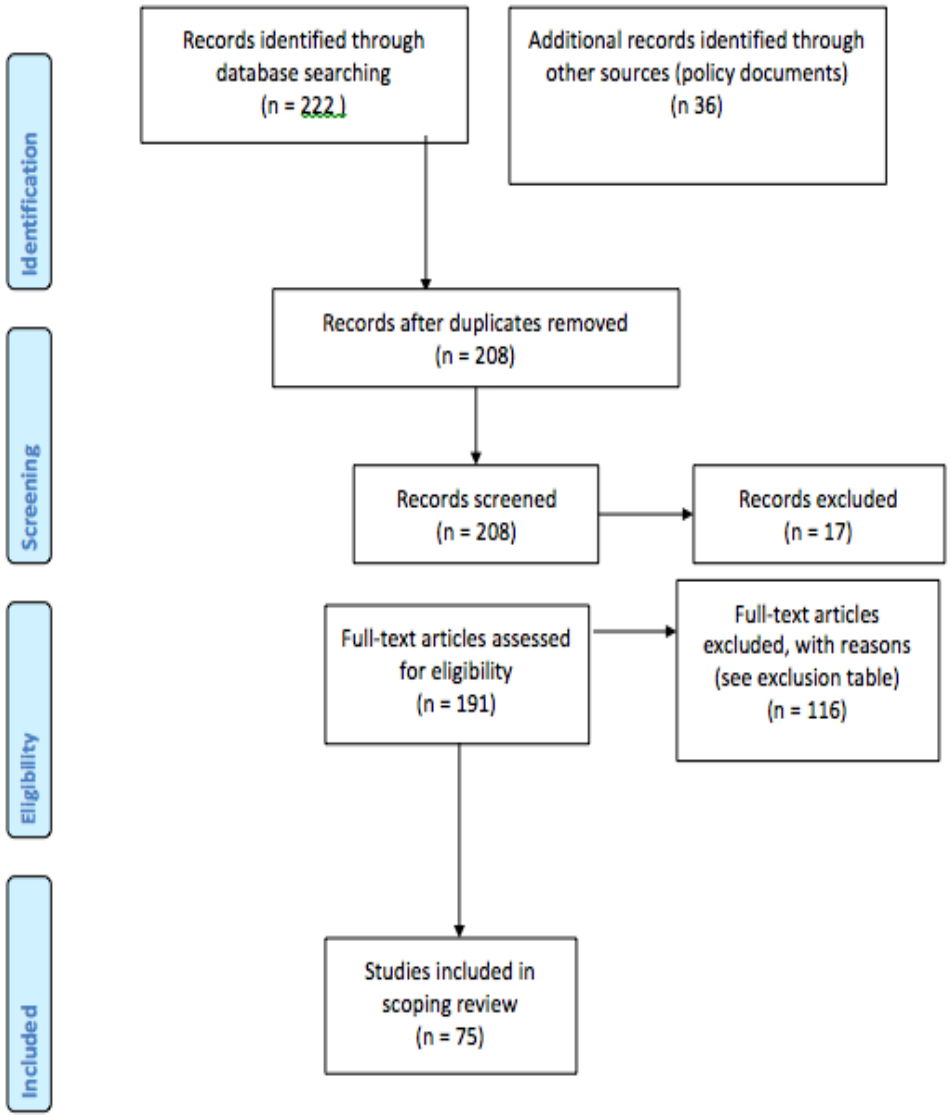
PSYCinfo search

1	Child	283133
2	Infant	34153
3	(child$ or infant$ or newborn$ or new-born$ or neonat$ or neo-nat$ or baby or babies or pediat$ or paediat$ or schoolchild$ or preschool$ or young$ or early life).ti	159440
4	(Multiple adj2 (need or needs or illness$ or disabilit$ or impairment$1 or impediment$1 or condition$1 or deficienc$ or diagnos$ or disadvant$ or problem$1 or condition$1 or syndrome$1 or disorder$1)).ti	899
5	(Congenital anomalie$ or congenital abnormalit$ or birth defect$).ti	97
6	(learning adj1 (difficult$ or disturbance$ or disability$ impairment$1)).ti	429
7	(Neurodisabilit$ or neurodevelopmental disorder$ or neurodevelopmental condtion$).ti	244
8	(Special educational need$ OR SEND NOT send or SEN not sen).ti	190
9	Complex need$.ti [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	627
10	(complex adj2 (need or needs or illness$ or disease$1 or disabilit$ or impairment$1 or impediment$1 or condition$1 or disadvant$ or problem$1 or syndrome$1 or disorder$1 NOT needle NOT needed)).ti	551
11	(definition$ or classification$ or meaning$ or criteria or categori#e$ or categori#ation$).ti	17797
12	(social adj1(class$ or exclusion or disadvantage$ or depriv$ or status$)).ti,ab.	8888
13	(Socioeconomic adj1(status or factor$ or position$)).ti,ab.	11629
14	(Health adj2 (disparit$ or inequality$)).ti,ab.	4025
15	(referral$ or hospital admission$ or care burden$ or community support or long term care or service utili#ation or care pathway or advance care planning[MeSH] or advance health care planning[MeSH]).ti	3570
16	1 or 2 or 3	317160
17	4 or 5 or 6 or 7 or 8 or 10	2395
18	16 and 9 (children with complex needs only)	243 (211)
19	16 and 17 and 11 (Children with complex needs and definitions)	7 (4)
20	12 or 13 or 14	23430
21	20 or 15	26946
22	16 and 17 and 21 (children with complex needs and other complications such as social class and multiple referrals.	20 (limits 19)
23	limit 18, 19 and 22 to (English language and yr="2005-current")	244 total.

Search strategy Medline

1	exp Child/	3496088
2	exp Infant/	1561338
3	(child$ or infant$ or newborn$ or new-born$ or neonat$ or neo-nat$ or baby or babies or pediat$ or paediat$ or schoolchild$ or preschool$ or young$ or early life).ti	2844593
4	(Multiple adj2 (need or needs or illness$ or disabilit$ or impairment$1 or impediment$1 or condition$1 or deficienc$ or diagnos$ or disadvant$ or problem$1 or condition$1 or syndrome$1 or disorder$1)).ti	15018
5	(Congenital anomalie$ or congenital abnormalit$ or birth defect$).ti	16013
6	(learning adj1 (difficult$ or disturbance$ or disability$ impairment$1)).ti	1358
7	(Neurodisabilit$ or neurodevelopmental disorder$ or neurodevelopmental condtion$).ti	1425
8	(Special educational need$ OR SEND NOT send or SEN not sen).ti	186
9	Complex need$.ti [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	189
10	(complex adj2 (need or needs or illness$ or disease$1 or disabilit$ or impairment$1 or impediment$1 or condition$1 or disadvant$ or problem$1 or syndrome$1 or disorder$1 NOT needle NOT needed)).ti	9304
11	(definition$ or classification$ or meaning$ or criteria or categori#e$ or categori#ation$).ti	294148
12	(social adj1(class$ or exclusion or disadvantage$ or depriv$ or status$)).ti,ab,kf.	42553
13	(Socioeconomic adj1(status or factor$ or position$)).ti,ab,kf.	79558
14	(Health adj2 (disparit$ or inequality$)).ti,ab,kf.	18944
15	(referral$ or hospital admission$ or care burden$ or community support or long term care or service utili#ation or care pathway or advance care planning[MeSH] or advance health care planning[MeSH]).ti	56121
16	1 or 2 or 3	4982117
17	4 or 5 or 6 or 7 or 8 or 10	43187
18	16 and 9 (children with complex needs only)	76 (limits 67)
19	16 and 17 and 11 (Children with complex needs and definitions)	71 (limits 30)
20	12 or 13 or 14	135328
21	20 or 15	190892
22	16 and 17 and 21 (children with complex needs and other complications such as social class and multiple referrals.	222 (limits 120)
23	limit 18, 19 and 22 to (English language and yr="2005-current")	217 in total

Appendix 2: PRISMA flow diagram for scoping review



Appendix 3: Methodological assessment of included studies for scoping review

Author	Aims of the Study	Methodology	Recruitment strategy appropriate?	Important results	Location/Trust/service type
(Aite et al., 2013)	Assess clinical pathways in which paediatric surgeons receive couples for prenatal consultation after prenatal diagnosis.	Emailed Questionnaires Quantitative analysis using fishers T-tests	Paediatric surgical centres	Sparse information is available about referral pathways to surgical specialists to the parents who receive diagnosis of surgically correctable malformations, and to the medical specialist who makes the diagnosis. Creation of referral guidelines is required.	Paediatric surgical units. Italian Nationwide
(Allsopp, 2006)	NA	Opinion piece	Children with complex health needs and disabilities	Development of a child passport identifying key and major needs of each child to improve coordination, reduce repetition for parents and improve efficiency of care pathways	Paediatric nurses and outreach nurses

(Áskelsdóttir et al., 2008)	Highlight experiences of parents who receive an antenatal diagnosis and prepare for admission to neonatal unit.	Qualitative interviews	Pregnant mothers who received an antenatal diagnosis.	A large time span exists between diagnosis and delivery. A coordinator needs to be appointed for the transition. Empathy towards prenatal mood and anxiety required.	Expectant mothers of a malformation. Canadian.
(Bachmann et al., 2009)	Reports main findings of the national evaluation of children's trust pathfinders	Prospective observational design. Mixed methods Questionnaires, case study's interviews	Children's services managers, directors and service planners. In both pathfinder and non-pathfinder areas.	This study showed improvements are based on public service values rather than profit incentives. Health services have been les involved than local authority education and social services. Children trusts have not yet brought about the radical change that was hoped for.	Local authority children services in England across different trusts.
(Baird, 2013)	Approaches to diagnostic classification systems.	Editorial	Neurodevelopmental disorders.	Children and young people with neurodisability frequently do not meet	On London based NHS hospital.

				specified diagnosis within the ICD-10 and the DSM-IV. ICD-11 and the DSM-5 are being revised. Promotion of quantitative approaches to symptom severity.	
(Beattie, 2000)	Service evaluation of a new service for children with complex healthcare needs.	Report – Qualitative semi-structured interviews with parent's and focus groups with professionals	Children with complex healthcare needs	Still in interim stages.	One UK NHS trust and one primary care group.(Beattie, 2000)
(Bettge et al., 2014)	Quantify relation between birth weight and special educational needs	Quantitative-logistic regression	Pooled data from 134313 children evaluated in 2007 – 2011.	Risk of SEN increased with moderately decreased birth weight. Other risk factors are social status.	Preschool examinations in berlin
(Bonanno et al., 2013)	Understand the emotional needs of parents who are expecting a child with a	Systematic review protocol	NA	NA	NA

	congenital anomaly.				
(Brombley, 2008)	Case examples used to demonstrate clinical and cost effectiveness of home care for children following ABI in the context of case management.	Case study	One child with acquired brain injury and his family	Demonstrates clinical and cost effectiveness of home care for children following acquired brain injury in the context of case management of intensive support.	One NHS trust in England. The South.
(Brooks et al., 2013)	Identify and descriptively map the key characteristics of the model of service delivery in operation, and to explore the user, carer and professional experience of service provision.	Case study – Qualitative interviews	Interviews with stakeholders and professionals in MDT teams.	Communication issues between professionals and with parents and children determine the quality of service provision.	Single site case study.
(Canyon, 2013)	Presents basic concepts of systems thinking and how it can be applied	Review	NA	Selection of enquiry models in paramount in systems thinking.	NA

	appropriately in health and social care.				
(Carnevale et al., 2008)	to investigate the needs of both the children and their parents with complex health needs	editorial	NA	Prevalence of children with complex healthcare needs can't be estimated due to different terms being used to classify these problems.	Canadian paper. Useful for definition of complex healthcare needs but not much else.
(Clarke, 2011)	Present new evidence on the ways in which multi-agency transition services meet the priorities and concerns of young people.	Qualitative interviews, quantitative survey	Managers and staff in five transition services, parents and young people receiving services.	A lack of service options exist for young people, particularly around employment, housing and leisure activities. There are substantial levels of unmet need among young people both pre- and post-transition. Unmet need appeared higher post transition than pre according to the mothers interviewed.	NHS Multi-agency transition services in England.
(Colver et al.,	Identify the features of	Longitudinal Cohort	450 young people with	Results not attained yet.	Outpatient clinics from

2013)	transitional care that are potentially effective and efficient for young people with complex healthcare needs making the transition.	study protocol	autism and another mental health condition, diabetes or Cerebral palsy		4 English hospitals.
(Colvin and Bower, 2009)	Create a record linkage of population-based birth defects registry and hospital discharge data to demonstrate the true burden of hospitalisation for children with Birth defects.	Population based. Retrospective.	Administrative data relating to all live births between the years of 1980 1999 and hospital discharges related to 1980-2000. Linked to birth defects registry. N=485, 446	While only 4.6% of live births in Western Australia were children with a major BD, this group accounted for 12% of hospital admissions.	Western Australian hospital discharge data
(Courtwright et al., 2011)	Compare age at death, intensity and cost of medical treatment for infants diagnosed pre or post natal with congenital anomalies	Retrospective cohort study	All features and neonates with congenital anomalies classified as lethal.	Highly aggressive interventions did not prolong survival and should not be offered.	North Carolina university hospital.

	considered to be lethal. Determine whether greater treatment intensity is associated with longer life.				
(Dale and Godsman, 2000)	Factors influencing GP referral to tertiary paediatric neurodisability service including reasons for referral, children's characteristics, and involvement of secondary specialist services.	Survey – Questionnaires	GPs referring children to a neurodisability service.	GPs are not contacting secondary services prior to referral. The majority of GPs (78%) were responding to parental concerns.	One neurodisability service in the UK.
(Doyle and Buckley, 2012)	A reflective account from a nurse working with children with complex healthcare needs.	Case study – reflective practice	Caring for children with complex healthcare needs in a home setting.		
(Dybwik et al.,	Explore experiences of	Qualitative	A family caring for other	High levels of dissatisfaction	Norwegian sample.

2011)	families giving advanced care to families requiring ventilation systems	Interviews	family members with complex health needs requiring home ventilation systems.	from families relating to support provided from community health services.	
(Ebela et al., 2011)	Analyse trend in mortality of infants and young people aged 0 to 4 years in relation to macroeconomic factors in Latvia and prevalence of congenital anomalies in new-borns in relation to socioeconomic factors	Correlation study	New born register and causes of death register	Strong correlation was found between child mortality and gross domestic product per capita, healthcare expenditures in Latvia per capita and unemployment.	Latvian sample. Highest child mortality in EU in practically all age groups.
(Elias et al., 2012)	Presents an approach to discharging children with complex medical needs with technology dependencies from hospital to home while addressing the needs	Clinical report.	Children with complex medical needs who are ready for discharge into the community.	A systematic approach to paediatric care is required with explicit care coordination; family centred care and advanced planning.	American academy of paediatrics.

	of the family.				
(Farasat and Hewitt-Taylor, 2007)	Reports on the evaluation of a pilot placement for preregistration of child health nursing students focused on supporting children with complex healthcare needs in their homes.	Service evaluation	Nursing students working in the community and hospital with children with complex health needs.	Pilot placement for nurses helped address many of the organisational and practical problems that can be taken as lessons learnt for the general professional care of children with complex healthcare needs.	Primary care trusts and PICU units in the UK
(Farel et al., 2003)	Examines the use of birth defects registers to identify and refer infants with birth defects and their families for early intervention services.	survey	Birth defects registers.	Birth defects surveillance programmes may be useful in locating children with complex healthcare needs, and referring them early to secondary services.	American, 50 states, district of Columbia and Puerto Rico.
(Fonseca et al., 2014)	Examines psychosocial adjustment of parents whose child has been diagnosed with a	Questionnaires	Parents with infant's who had a diagnosis of children with a CA.		Hospital based data from one hospital in Portugal.

	congenital anomalies				
(Furness et al., 2009)	Explore in depth attitudes of hospital paediatric staff caring for children with multiple unexplained physical symptoms	Questionnaires	128 Health professionals working in paediatric hospital.	Clear desire by NHS staff for more information and training from psychiatric services to help prepare for this group.	One large hospital NHS trust in England
(Gangadharan et al., 2001)	Describe the nature of disabilities of children referred to child learning disability team	Questionnaires	Child outpatients over a period of 8 months. N=63	The need for a team with specialist skills in mental health problems as secondary is needed.	Dedicated service for children with learning disabilities in Leicestershire UK
(Hefner, 2011)	Healthcare utilisation of children with complex healthcare needs and demographic patterns	Dissertation – Factor analysis	Children with special healthcare needs	Children with complex healthcare needs have a higher likelihood of negative outcomes those children whose needs are less complex.	American healthcare system.
(Hewitt-Taylor, 2005)	Create a broad description of the perceived education and training needs of	Survey – quantitative	Children's hospices in the UK, organisations on the national list of providing respite care,	Children with complex medical and technical needs are cared for by a variety of different healthcare	UK primary care trusts, respite centres and children's hospices.

	those who care for children with complex healthcare needs.		children's community nursing teams within local primary care trusts. 60% response rate to questionnaire	professionals and specialist training is required.	
(Hewitt-Taylor, 2008b)	Explores parent's perceptions of their children who have complex health needs and their experience of communication, play, socialising and learning.	Survey – qualitative questionnaires with parents.	Mothers with children with complex healthcare needs.	Parents felt that their child's efforts to communicate were not valued. Parents reported a mixed experience of inclusion in education settings.	Organisations non-NHS in the UK
(Hewitt-Taylor, 2008c)	Discusses the experiences of mothers with children with complex health needs in relation to their child's hospitalisation.	Case study and semi-structured interviews.	13 mothers and 2 fathers whose children have experienced hospitalisation.	Parents are concerned about staffing levels on Paediatric wards, which require them to step in to care for their child.	One hospital in England.
(Hewitt-Taylor, 2009c)	to gain understanding of healthcare staffs	Qualitative – Semi-structured	No – not staff from NHS and only one area for	Working in people's homes is rewarding due to the	Staff from various organisations, which

	experiences of providing home care to children with complex healthcare needs	interviews	not generalizable. Anecdotal only.	intimacy and strong rapport building with clients. In the same way challenging to reflect a helpful, rather than intrusive approach.	were not NHS.
(Hewitt-Taylor, 2009c)	Gain an in depth understanding of heath care staffs experiences of working with children with complex healthcare needs.	Qualitative – semi-structured interviews.	14 staff from a range of different organisations not including NHS staff.	Staff needs to form relationships with families that are supportive rather than intrusive, respecting family's choices while working within professional boundaries.	A range of Non-NHS organisations in England
(Hewitt-Taylor, 2012a)	Describes development of a programme of learning aimed at meeting the needs of healthcare assistants who provide support for children with complex healthcare needs.	Case study	Healthcare assistants working with children with complex healthcare needs.	The university which piloted the training programme adopted it as an official qualification	One university in the south of England.
(Hewitt-Taylor,	Understand how the	CPD piece –	CPD reflection on	Although the child's needs	One university in the

2012b)	plan the hospital discharge of a child with complex health needs	reflection	practice by university lecturer.	should be central in DC planning, it should be within the context of the family.	south of England
(Hobson and Noyes, 2011)	Analyse the roles of fathering for children with complex healthcare needs.	Qualitative interviews.	8 Fathers who have children with complex healthcare needs under a child community nursing team	Performing intimate care proves challenging for fathers. Specific services may be required	One child community nursing team in England.
(Kirk and Glendinning, 2002)	Describes elements of professional support that were particularly valued by parents of children with intensive and complex healthcare needs.	Qualitative face to face interviews.	23 mothers and 10 fathers of technology dependent children now being supported at home.		Specialist children's hospitals in the UK
(Kirk, 2001)	Assess how the transfer of responsibility from professionals to parents was negotiated when children with	Qualitative – In depth interviews.	23 mothers, 10 father's 44 professionals caring for children and supporting families in the community.	Professional's expectations of parental involvement in the care of sick children can act as a barrier to negotiation of roles.	Three children's hospitals within the UK.

	complex healthcare needs are discharged into the community.				
(Kirk, 2008)	How young people with complex healthcare needs experienced different transitions.	Qualitative interviews	28 young people aged between 8-19 from community children's nursing teams.	Young people with complex health needs may have requirements which adult services are not prepared for.	Community child nursing teams in the north west of England.
(Knapp et al., 2008)	Quantify the costs to young disabled people and their families to identify the societal economic impacts arising from these challenges.	Literature review	UK research, policy and birth cohort data.	There are not enough funds being spent on disabled children and young people to enable those who reach adulthood to fulfil their ambitions.	UK research, policy and cohort data.
(Kuo et al., 2011)	To profile national prevalence of more complex children with special healthcare needs and the diversity of caregiver challenges	Cross sectional secondary analysis	2005-2006 national survey of children with special healthcare needs (n=40,723)	Families with more complex special healthcare needs report multiple unmet needs and high demands placed on their family members.	United states based population

	that their families confront.				
(Kurinczuk et al., 2010)	Provide a background to the evidence review process by examining the contribution of congenital anomalies to infant mortality rate associated with congenital anomalies.	Project briefing	Review of congenital anomalies surveillance systems/literature review	Congenital anomalies contribute about one third of the extra infant deaths experiences by routine and manual groups compared with the population as a whole.	Literature and congenital surveillance systems in the UK
(Law et al., 2011)	Investigates the role and activities of nursing and allied health professionals caring for children with complex healthcare needs in a community setting.	Qualitative interviews and focus groups	Nurses and Allied health professions within health boards in the UK representing public health nursing, health visiting, school nursing, looked after children's nursing, speech and language therapy.	Findings support adoption of integrated partnership working, going beyond the identification of key professionals, to develop a set of criteria against which future service provision could be judged.	UK based within four health boards in Scotland
(Lenton et al.,	Discuss the overlapping	Editorial	Opinion piece	Questions are raised about	UK

2004)	boundaries between complex healthcare needs, children with disability, palliative care and technology dependence.		Children's nursing research. Editorial for a special edition of Child: Care, Health and Development.	the nature and type of provision required by children and families who have long-term conditions and the interface between disabled children services and palliative care.	
(Looman et al., 2013)	Describe the value of the advanced practice nurse's enhanced scope of knowledge and practice for relationship-based care coordination in healthcare homes that service children with complex special healthcare needs.	Case study	Advanced practice nurses in America.	Having a lead coordinating advanced practice nurse is likely to reduce fragmentation of care for children with complex special health care needs.	US based study.
(MacDonald and Callery, 2004)	How is respite defined for groups of parents, nurses and social	Interviews	19 mothers and 7 fathers of children requiring complex care.	Appropriate provision of respite care and communication with parents	Schools, respite facilities and community data bases of special

	workers responsible for caring for children with complex healthcare needs.			requires understanding of the meaning of respite to patents.	needs children in the North of England.
(Magana and Smith, 2008)	Examine health behaviours, utilization and access to care among older Latina and black American mothers who co-reside with a child with developmental disabilities.	Cross sectional	162 Latina and black American mothers with children with a developmental disability. Selected from the National Health Interview Survey 2005.	Disability services providers needs to address the mental and physical healthcare needs of the family caregivers in addition to those of the child with disability	Latina and black American mothers from the UK.
(Manhas and Mitchell, 2009)	Ethics of proximity and why ethics are relevant for one child's with complex healthcare needs when going home.	Case study	1 child with complex healthcare needs returning home.	During periods of transition, children with complex healthcare needs benefit from close proximity and contact with social support networks and experts.	
(Maybery et al., 2012)	to identify the key goals that are established	Cross sectional	Healthcare plans of 44 parents and 41 children	Goal setting appears to be an important approach to	Australian study.

	By children and parents from families in which parents have substance use and/or mental health problems.		classed as complex families.	direct and motivate parents and children where the parents have psychiatric or other disabilities.	
(McCann et al., 2012)	Critically examine research that quantifies and describes daily patterns of time use by parents of children with complex healthcare needs	Systematic review	32 studies in English or French language incorporating children with complex healthcare needs and a quantitative measure of time use.	Parents with complex healthcare needs carry a significant caregiving burden that often does not reduce as the child's age increases.	Australian study. Used international databases to find literature. Not confined to Australian studies only.
(Morales-Surez Varela et al., 2009)	Investigate association between socioeconomic status and the frequency of major congenital anomalies in offspring.	Cohort study	81435 live singletons born to mothers, 3352 cases of major congenital anomalies were identified by linkage to the national hospital discharge register.	An association exists between low socioeconomic status and cases of congenital anomalies.	Danish national cohort study

(Morales-Surez Varela et al., 2009)	Investigate the association between socioeconomic status and the frequency of major congenital anomalies in offspring.	Cohort study	3352 cases of congenital anomalies cases (EUROCAT criteria) were identified by linkage to the National Hospital Discharge Register.	Prevalence of all recorded major congenital anomalies was similar, about 4% in all socio-occupational categories. Low socioeconomic status did correlate with a higher prevalence of congenital anomalies of the respiratory system, the heart and circulatory system.	Danish national cohort study. Danish population.
(Narramore, 2008)	The review highlights factors affecting parents' emotions and discusses how early support, home visits and Practical help can all help to alleviate parents' emotional stress.	Literature review	Recognized academic electronic databases to search for articles and Research papers published within the last five years. Recent British government papers were also reviewed as part of the literature search.	Early provision of support is essential. Father's emotional needs are often overlooked.	UK based governmental literature and research.

(Nicholl and Begley, 2012)	Explore experiences of a group of mothers who were caring for children with complex healthcare needs, including those with life-limiting illnesses at home.	Qualitative to Interviews	17 mothers in Ireland caring for children with complex healthcare needs.	Mothers caring for children at home require trusting relationships from professionals and support from effective interventions.	Mothers with children with complex healthcare needs in Ireland.
(Nicholl et al., 2013)	Determine the types of technology used by children with complex healthcare needs cared for by their parent's at home.	Mixed methods survey. Questionnaires	9 Expert nurses providing home respite to children up to 4 years of age with complex healthcare needs. 177 Parents in receipt of services also sent questionnaires.	Informs practitioners of the specific types of technology in use within the home and could be particularly useful for discharge planning teams in the acute setting.	One voluntary organisation in Ireland specialising in support for children with complex healthcare needs.
(Oulton and Heyman, 2009)	Explore the risk perception of parents caring for children who have severe learning disabilities and complex	Qualitative interviews. Cross sectional	20 Parents of children with severe learning disabilities. Participants came from 7 countries.	Although parents sometimes temporarily transferred caring duties to others, they usually retained a sense of anxious responsibility for	London based special schools catering for children ages 3-19 years.

	medical needs.			such care, supervising or auditing the activities of other carers rather than delegating risk ownership.	
(Peter et al., 2011)	Evaluation of an ambulatory care coordination program for children with complex care needs.	Cross sectional service evaluation.	101 children enrolled in a tertiary paediatric hospital	A systems approach is required to provide a service for children with complex healthcare needs, crossing the child's journey from the home to hospital.	One tertiary service in western Australia.
(Pratt et al., 2012)	Findings from an audit and change management process for the patients experience of hospital admission for people with learning disabilities.	Audit – Service improvement	Audit to families and hospital staff.	Preplanning that involves the family with a dedicated informed staff member can dramatically reduce distress and improve the patient and staff experience.	One tertiary service in the UK.
(Reichman et al., 2008)	Provides an overview of the impact of disability on the family and the	Commentary	Paediatrician's commentary on the impact of disability on	More research is required into the economic pathways and service utilisation for	US study

	range of complex healthcare needs		children and families	children with complex healthcare needs.	
(Runciman and McIntosh, 2003)	Reports the results of an external independent evaluation of parents and agency member's perceptions of the partnership and training supporting children at home (PATCH) service.	Qualitative – Semi-structured interviews	10 families selected from the project that have a child with complex healthcare needs.	The freedom to work flexibly and approach agencies directly and the ability to cut across established organisational structures were significant factors in improving support for families.	One service in Scotland of a specialist nursing services.
(Sartore et al., 2013)	Protocol for a systematic review to assess the effects of peer support interventions on a range of psychological and psychosocial outcomes for parents of children with complex healthcare needs.	Systematic review protocol.	Studies reporting on parents and carers of children with complex healthcare needs, where complex healthcare needs include chronic or sever acute illness, disability or delayed atypical development in the	NA	All studies meeting the author's inclusion exclusion criteria.

			physical, psychological, developmental, or intellectual domains.		
(Stoll et al., 2002)	Describe the impact of prenatal diagnosis on the birth prevalence of congenital anomalies over 21 years (1979 – 1999) in a well-defined population in north eastern France.	Cross sectional?	279,642 consecutive births of known outcome registered in a congenital anomalies register covering 11 maternity hospitals for the period 1979-1999	Large differences in detection rate of types of congenital anomalies and in the rate of termination of pregnancy. Prenatal diagnosis of congenital anomalies of significantly higher when associated malformations are present.	Once city in France and urban area and the surrounding rural area around Strasbourg.
(Sutton et al., 2008)	Determine whether an ED-based advice and coordination programme was feasible and could prevent or accelerate ED care for these patients.	Prospective – cross sectional survey	Patients who attended emergency departments more than 4 times over a 12 month period. Piloted in 2002, ran until 2006.	Through a comprehensive programme including the development of patient-care plans, care coordination and 24-hour mobile phone access family's capacity to manage their children's conditions in the community were enhanced.	One large tertiary children's hospital in Melbourne.

(Tait, 2002)	Determine the extent to which the aims of a pilot project to set up service coordination had been met.	Qualitative – interviews, focus groups.	25 families referred to the project with children with complex healthcare needs.	In order for any service coordination strategy to work, it needs to be universally constructed and agreed.	One city on England,
(Tan et al., 2012)	Prospectively describe the bereavement experience of parents whose infants die in acute care settings with a complex chronic condition	Longitudinal qualitative interviews.	2008-2011 data collected as part of a case study exploring parent and healthcare provider decisions making. 72 narrative interviews from 7 cases, which was 14 parents of 8 infants who had died.	Anticipatory support prior to the death of an infant assists with smoother transition to coping with death.	US academic medical centre
(Thurgate, 2005)	A review of the literature to discuss the differing needs of respite care for children with complex healthcare needs	Literature Review	Audit of respite services for children with complex health needs in one hospital trust	Despite a number of government incentives stating respite for children with complex healthcare needs is required, there is limited evidence to support	East Kent hospital trust

				this.	
(Thurston et al., 2010)	Explore interactions between child and parents psychological factors and team integration variables that may explain improvements in the quality of life for children with complex healthcare needs.	2-year longitudinal survey.	Families with children 0 to 19 years of age, living in one particular town in Canada, with multiple needs.	Rehabilitation providers working with children with complex healthcare needs and their families should also address child and parent problematic behaviours.	Canadian study.
(Ungar et al., 2014)	Explore how multiple service using youths with complex healthcare needs exposure risks are increased by uncoordinated services.	2 Case Studies and Literature review	Young People with Complex health needs (YPCN) – Psychological disorders and social circumstances.	YPCN require multi-level coordinated services that they require some input into designing. Further research needed about patterns of services provision over time and service configuration. 6 principles of best practice suggested for services for YPCN.	Atlantic Canada. Psychosocial services

(Wang et al., 2009)	To quantify the effect of socioeconomic status on health outcomes during the first year after new born discharge among infants with complex chronic conditions (CCC).	Longitudinal, population-based cohort study.	512 768 infants at DC from new-born hospitalisation. 2.3% had CCCs identified during new-born hospitalisation.	SES related inequality affects hospitalisation and possibly mortality rates among medically vulnerable infants.	Ontario Canada. Data taken from 2 administrative databases.
(Watson et al., 2002)	Examines literature on barriers to disabled children and the need for multiagency working.	Literature Review	UK literature governmental and research on children with complex healthcare needs and service coordination	Providing the legislative conditions to foster multi-agency working is not in itself enough to bring about truly effective support for families and children. Ongoing field work is required.	UK study
(Watson et al., 2011)	Identify successful models of transitional care for young people with complex heath	Scoping review to allow a wide variety of policy and literature	Young adults, teenagers in transition of services, with CP, ASD or Diabetes.	No models of transitional care exit for young people with ASD. Services lack evaluation.	UK NHS and political evidence.

	needs.			Normalization theory process provided structure to assess key elements required for implementation and integration of new practice into everyday healthcare.	
(Whiting, 2013)	Identify areas of consistency and of difference in parental experiences of caring for a child with disability or complex healthcare needs.	Interviews qualitative	34 parents of children with complex healthcare needs or disabilities from 33 families, 11 families	Major areas of consistency within the experiences of parents of children with life-limiting condition, disabilities and technology dependence were found.	England. Two NHS hospital trusts three local primary care trusts and local non-NHS children's hospice.
(Whiting, 2014)	Investigate the experiences of parents of children with complex health needs in relation to the help and support they	In depth semi-structured interviews.	Interviews undertaken with parents of 34 children with a disability or a complex health need.	Parents identified a range of healing behaviours among key professional staff involved in support provision. The greatest area of unmet needs is for respite	Four NHS trusts in England and one children's hospice.

	receive when caring for their child.			care.	
(Woodgate et al., 2012)	Extend understanding of how changing geographies of care influence ways that Canadian families with children with complex healthcare needs participate in everyday life.	Longitudinal qualitative	Families recruited from primary integrated health and social services community agency located in Canada. 68 parents, which included 41 children with complex care needs. Age range of between 6 months to 26 years. 9 of the children had cerebral palsy.	Enhanced participation of families was dependent upon the family's ability to harness resources in a physical sense such as technology and equipment, but social interaction.	Canadian study
Carter, Cummings, Cooper (2005)	Yes – Exploring multiagency working practice using appreciative enquiry.	Appreciative interviews with mothers and children who have experienced complex care	No to Purposive sampling (biased due to Geographic's) and snowball sampling. Also biased. 20 families from two areas in	Yes – 10 key best practice statements Yes – The workshops have been mirrored at other trusts and conferences. Limited to geographical area.	Two counties in UK represented by workforce development confederation.

			Burnley to represent two health economies.		
Woodgate, Edwards, Ripat (2012)	Yes – Longitudinal ethnography to understand how changing geographies of care influence the ways families with CCN participate in everyday life	Open ended interviews allow scope for explaining experiences.	Biased sampling technique (purposive and snowball)	Yes – 4 main themes identified from interviews. Yes – Explores meanings of family members. No – based in Canada, and parents experiences need to be reflected in organisational change.	Canadian Study

Appendix 4: Scoping review detailed exclusion criteria

Name of paper	Reason for exclusion
(Bethell et al., 2012)	Related to school management rather than healthcare.
(Bower et al., 2009)	Age at diagnosis of birth defects. Not related to care pathways or definitions of complex healthcare needs.
(Carlson et al., 2008)	Based primarily on childhood cancer survivors who are likely to receive different support/already known to services.
(Chapman et al., 2011)	Specifically related to timing of diagnosis of congenital hearing loss. Too specific and not related to service provision or definitions of complex healthcare needs.
(Chen et al., 2007)	Based in Taiwan and specifically related to diagnosis of neurodevelopmental disorders. No definitions of complex healthcare needs or evaluation of health service systems that is geographically relevant.
(Clarke and Houlihan, 2005)	Sample not representative. Specific to referring children to psychological services rather than over all pathway analysis. Focuses on learning disability rather than all complex healthcare needs.
(Colvin and Bower, 2008)	Poster presentation with minimal information
(Dastgiri et al., 2003)	Focused on survival of children diagnosed with congenital anomalies, not related to service evaluation or definition of complex healthcare

	needs.
(Egilson, 2011)	Related to physical therapy only. Not broad enough to be relevant for complex healthcare needs. Relates to therapy services only.
(Emerson et al., 2012)	Editorial, Not methodologically strong enough to draw conclusions from findings.
(Fenton and McFarland-Piazza, 2014)	Focuses on implementation of a specific intervention approach rather than focusing on the children who will be receiving it.
(Flanigan and Wolff, 2012)	Conference abstract. Not methodologically sufficient to make judgements.
(Flitton and Buckroyd, 2005)	Age group to high. Specifically related to counselling of one child.
(Forbes et al., 2007)	Too generic about the role of the nurse across children's services. Does not analyse role in complex healthcare needs.
(Franck, 2004)	Commentary piece only. Not methodologically strong enough for analysis
(Harlap et al., 2008)	Population sample not relevant.
(Hewitt-Taylor, 2008a)	Opinion – not methodologically strong enough.
(Hewitt-Taylor, 2009a)	Specifically related to schooling of children with complex healthcare needs. No mention of meaning of the term.
(Hewitt-Taylor, 2009b)	Review, not methodologically strong enough
(Karmiloff-Smith et al., 2012)	Focuses on neuropsychological models applied to genetic and

	environmental vulnerabilities in children. Does not discuss service utilisation.
(Kaurstad and Bachmann, 2014)	Poster abstract only. Not methodologically strong enough
(Mazzotti et al., 2013)	Specific to low birth weight only, does not focus on complex healthcare needs as a result of low birth weight.
(McCracken and Pettitt, 2011)	Related specifically to deaf children. Is also a report. Not a research study.
(McDonald et al., 2007)	Specifically related to seating equipment provision.
(Mitchell, 2011)	Main focus of paper related to application of evidence based practice. Also classifies children as complex healthcare needs as psychosocial issues and substance misuse issues only.
(Morris et al., 2013)	Specifically related to a definition of neurodisability.
(Nowicki et al., 2014)	Not relevant topic. About social exclusion and children's perceptions of this with learning difficulties. No discussion of complex healthcare needs.
(Raeburn, 2013)	Opinion piece – Found original paper cited and used instead.
(Reading, 2003)	Report of a research article. Not methodologically strong enough.
(Reber et al., 2011)	Related to parental drug addiction and complications related to child. Not relevant.
(Reupert and Maybery, 2014)	Focuses on parents who have mental health problems and complex healthcare needs. Not children.

(Rouhani et al., 2007)	Not related to complex healthcare needs, and no comparisons can be made to the health service in UK as the study is based in Spain
(Tennant et al., 2010)	No definition of complex healthcare needs or discussion of healthcare utilization. Focuses on survival time of children with specific congenital anomalies
(Ungar et al., 2012)	Age of child too high – Canadian setting, health service layout different to UK
(Yampolskaya et al., 2006)	Related to children in an out of home care service specific to one region in Canada, for children who have suffered abuse.

Appendix 5: Definitions of complex healthcare needs in children extracted from scoping review

Yellow – Technology dependent

Blue – Requiring psychological input

Green - Requires more than one service provider

Red – Indicating long-term need for services

Name of paper	Definition
Watson et al. (2011)	Young people with complex health needs (CHNs) Those with or mental health impairment with the potential for substantial and long-term adverse effects on their ability to carry out normal day-to-day activities.
Watson et al. (2002)	Disabled children with complex healthcare needs typically require technical and or medical equipment in the home, both because of their need for intensive ongoing care, and to compensate for the loss of a vital bodily function, such as the ability to breathe or feed independently.
Carter et al. (2007)	A diverse group of children, who are medically fragile, or technologically dependent, require high levels of physiological, psychological, social and educational care and support, bringing them into therapeutic contact with a wide range of different professionals and people from other agencies.
Woodgate, Edwards, Ripat (2012)	A group of children with complex care needs who have disabilities and often are dependent on assistive or medical technology.
(Ungar et al., 2014)	Children with very complex healthcare needs living in adverse environments and with multiple bio-psychosocial barriers

	to growth, social service system design and resilience.
(Beattie, 2000)	Children with complex healthcare needs – Under the age of 8 and has a significant health-related condition, which means than he/she requires specialist services from at least more than one service.
(Hewitt-Taylor, 2009c)	When a child has complex healthcare needs, it is necessary for their family to have day-to-day assistance to enable them to live at home.
(Brooks et al., 2013)	Children with discrete needs caused by a condition that is usually lifelong and who require additional support from more than one agency are categorised as children with complex healthcare needs. Thus there is no agreed definition of complex healthcare needs/conditions.
(Carnevale et al., 2008)	Children requiring life-support technologies that stem from multi-organ system involvement.
(Colver et al., 2013)	Young people with complex health needs are those with a physical, mental or health impairment that has the potential for a substantial and long-term adverse effect on their ability to carry out day-to-day activities.
(Doyle and Buckley, 2012)	Children with complex healthcare needs are likely to be technology dependent, and require medical nursing care for life, which may include ventilation, enteral feeding and intravenous drug administration. Some children have multiple disabilities requiring continuing interventions.
(Elias et al., 2012)	Problems faced by families that are complex, include significant feeding and respiratory problems, often associated with technology dependencies. They may also have intellectual disabilities, physical impairments, and sensory deficits that require specialised therapeutic and educational interventions.
(Elias et al., 2012)	Children with a medical complexity: Substantial healthcare needs, 1 or more chronic conditions, functional limitations often associated with technology assistance and healthcare use.
(Farasat and Hewitt-	Children with tracheostomies, those who require long-term assisted ventilation, Oxygen therapy, assisted enteral or

Taylor, 2007)	parental feeding, dialysis, administration of intravenous drugs, and while technical and medical needs can be stabilised by interventions, not letting these requirements detract away from the psychosocial, emotional and developmental needs to allow then to live in the community.
(Hefner, 2011)	A term used to describe a child's ongoing healthcare needs, including the required number of providers, the diversity of the types of providers and the frequency of provider contacts.
(Hewitt-Taylor, 2008b)	Children with complex healthcare needs require daily interventions, ongoing technical and medical support, such as assisted ventilation, oxygen therapy, gastrostomy feeding and may have associated problems such as speech, vision, or mobility difficulties.
(Hewitt-Taylor, 2012a)	Children who require long-term assisted, ventilated oxygen therapy, tracheostomy care and assisted feeding, meeting the child's social, emotional and developmental needs as well as physical needs and the needs of their families.
(Hewitt-Taylor, 2010)	Children who require long-term oxygen therapy and or assisted ventilation and feeding, and those who have prolonged and difficult to manage seizures. These children may also have problems with their speech, hearing or mobility. Some may have a learning disability.
(Hewitt-Taylor, 2012b)	Children who are dependent on technology and those who require a significant amount of additional care. Among these children are those who require long-term assisted ventilation, oxygen administration and gastronomy feeds.
(Hobson and Noyes, 2011)	Children with complex health needs include those requiring tracheostomies, long-term ventilation, assisted enteral or parenteral feeding, administration of intravenous drugs, and may include children with severe movement disorders or mobility impairments, some children have sensory impairments.
(MacDonald and Callery, 2004)	Severely disabled children who require complex healthcare at home.

(Maybery et al., 2012)	Families with complex healthcare needs: Reduced parenting capacity, poorer family dynamics and lower child wellbeing. Parents have at least one mental health problem or one substance misuse problem.
(McCann et al., 2012)	A child with complex healthcare needs has at least one group of primary care givers of children who were described as having congenital anomalies, intellectual or physical impairment, and /or a chronic illness.
(Looman et al., 2013)	Children with medical complexity – Characteristic patterns of family-identified healthcare service needs, Lifelong chronic conditions that are severer and/or associated with medical fragility, functional limitations that may be severe, requiring assistance from technology, and high utilisation of health resources such as hospitalisations and/or the involvement of multiple subspecialists.
(Kelly et al., 2008)	Children with special healthcare needs (CSHCN) have varied conditions, each requiring diverse resources. Those who have or are at increased risk for chronic physical, developmental, behavioural or emotional conditions and who require health and related services of a type or amount beyond that required by children generally.
(Kuo et al., 2011)	Children with special healthcare needs (CSHCN) are clinically recognised by at least one chronic condition resulting in high family-identified service need, medical equipment addressing functional difficulties, multiple subspecialist involvement and elevated health service use.
(Peter et al., 2011)	Children with special healthcare needs (CSHCN) in the US encompasses those with congenital, acquired, and developmental/behavioural condition, degrees of chronicity, technology, and care dependence or limitations in activity. Those children with chronic conditions that involve several organ systems and/or require multiple specialists, technological supports, and community services.
(Sartore et al., 2013)	Children with any acute or chronic medical or psychological condition with relatively long-lasting course or sequel.
(Nicholl et al., 2013)	Require complex intervention that are ongoing rather than requiring acute intervention, thus increasingly dependent on

	equipment or technological devices to sustain life or optimise health and have the need for substantial and complex care for substantial parts of the day or night.
(Nicholl and Begley, 2012)	Those with life-limiting or life-threatening conditions, disabilities and chronic illness.
(Wang et al., 2009)	Complex chronic conditions (CCC) any medical condition that can be reasonably expected to last at least 12 months and to involve wither several different organ systems of 1 organ system severely enough to require speciality paediatric care and probably some period of hospitalisation in a tertiary care centre.

Appendix 6: Search strategies for study 1

Key terms search for GP databases Medline

1	“congenital anomal$”	10063
2	“congenital abnormalit$”	12107
3	“congenital defect$”	2130
4	“congenital birth defec$”	179
5	“birth defect$”	6131
6	“congenital malformation$”	0
7	“birth injur$”	1891
8	“congenital deformit$”	461
9	“general practic$”.ti,ab,kf	18125
10	“GP”.ti,ab,kf	26380
11	“primary care”.ti,ab,kf	71289
12	“the health improvement network”.ti,ab,kf	402
13	“the general practice research database”.ti,ab,kf	1027
23 – Congenital anomalies	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	21573
24 – GP related	9 OR 1O OR 11 OR 12 OR 13 OR 14	164724
25	23 AND 24	168
26	Limit to English language and human studies	149

MeSH terms search for CA registers PubMed

1	Congenital anomalies/epidemiology [MeSH]	531626
2	Consanguinity [MeSH]	12107
3	1 AND 2	111

Key terms search for CA registers Medline

1	“congenital anomal$”	10063

2	“congenital abnormalit$”	12107
3	“congenital defect$”	2130
4	“congenital birth defec$”	179
5	“birth defect$”	6131
6	“congenital malformation$”	0
7	“birth injur$”	1891
8	“congenital deformit$”	461
9	“the clinical practice research datalink”.ti,ab,kf	433
10	“BINOCAR”.ti,ab,kf	4
11	“EUROCAT”.ti,ab,kf	176
12	“British and Irish network of congenital anomaly researchers”.ti,ab,kf	0
13	“European surveillance of congenital anomalies”.ti,ab,kf	50
14	“disease register$”.ti,ab,kf	264
15	“disease registr$”.ti,ab,kf	1034
16	“Disease register$”.ti,ab,kf	264
17	“disease registr$”.ti,ab,kf	1034
18 – Congenital anomalies	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	21573
19 – Registers	9 OR 10 OR 11 OR 12 OR 13 OR 14	1491
20	18 AND 19	118
21	Limit 20 to English language and human studies	96

Maternal risk factors search Medline

1	“congenital anomal$”	10063
2	“congenital abnormalit$”	12107
3	“congenital defect$”	2130
4	“congenital birth defec$”	179
5	“birth defect$”	6131
6	“congenital malformation$”	0

7	“birth injur$”	1891
8	“congenital deformit$”	461
9	“Maternal risk factor$”.ti,ab,kf	52
10	“pregnancy exposure$”.ti,ab,kf	246
11	“Neonatal risk factor$”.ti,ab,kf	222
12	“Neonatal exposure$”.ti,ab,kf	833
13	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	21573
14	9 OR 10 OR 11 OR 12	1615
15	13 AND 14	67
16	Limit 32 to (English language and humans)	63

Appendix 7: Search strategy comorbidities and disease severity

Medline and CINAHL search

Multi-morbidity measures

1	“measure$”.ti	127785
2	“assessment$”.ti	153780
3	“score$”.ti	23165
4	“tool$”.ti	48312
5	“classification$”.ti	31563
6	“index$”.ti	38681
7	“outcome$.ti	191014
8	“record$”.ti	25931
9	“multi-morbid$”.ti	65
10	“co-morbid$”.ti	451
11	“comorbid”.ti	11258
12	“disease severit$”.ti	2597
13	“disease count$”.ti	16
14	“multimorbidit$”.ti	648
15	“primary care”.ti	26750
16	“communit$ healthcare”.ti	68
17	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	609544
18	9 OR 10 OT 11 OR 12 OR 13 OR 14	14994
19	15 OR 16	26817
19	15 OR 16	22

Child comorbidity measures

1	“measure$”.ti	127785
2	“assessment$”.ti	153780
3	“score$”.ti	23165
4	“tool$”.ti	48312
5	“classification$”.ti	31563
6	“index$”.ti	38681
7	“outcome$.ti	191014
8	“record$”.ti	25931

9	“multi-morbid$”.ti	65
10	“co-morbid$”.ti	451
11	“comorbid”.ti	11258
12	“disease severit$”.ti	2597
13	“disease count$”.ti	16
14	“multimorbidit$”.ti	648
15	“child$”.ti	340209
16	“infant$”.ti	73027
17	“newborn”.ti	15746
18	“new-born$”.ti	162
19	“neonatal”.ti	39575
20	“neonat$”.ti	53918
21	“neotonatal”.ti	9
22	“bab$”.ti	12267
23	“Paediat$”.ti	14770
24	“pediat$”.ti	74248
25	“Young”	65874
26	“early life”.ti	2819
17	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	609544
18	9 OR 10 OT 11 OR 12 OR 13 OR 14	14994
19	15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26	615769
19	17 AND 18 AND 19	75

Appendix 8: NHS research passport approval letter

Bradford Teaching Hospitals NHS
NHS Foundation Trust

Bradford Institute for Health Research
Temple Bank House
Bradford Royal Infirmary
Duckworth Lane
Bradford
West Yorkshire
BD9 6RJ
Tel: 01274 383418

17th November 2015

Christine Bishop

BY EMAIL

Dear Christine

LETTER OF ACCESS FOR RESEARCH

Study: Service Utilisation – Born in Bradford
REDA No: 885
POC: Rosie McEachan

If you have not already provided your ID documentation to Sadia Khaliq please do so on the day you start work at Bradford – this is a term of your Letter of Access*

This letter should be presented to each participating organisation before you commence your research at that site.

In accepting this letter, each participating organisation confirms your right of access to conduct research through their organisation for the purpose and on the terms and conditions set out below. This right of access commences on 17 November 2015 ends on 17th November 2018 unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from Bradford Teaching Hospitals NHS Foundation Trust. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving confirmation from the individual organisation of their agreement to conduct the research.

The information supplied about your role in research at the organisation has been reviewed and you do not require an honorary research contract with the organisation. We are satisfied that such pre-engagement checks as we consider necessary have been carried out. Evidence of checks should be

available on request to the organisation.

You are considered to be a legal visitor to the organisations premises. You are not entitled to any form of payment or access to other benefits provided by the organisation or this organisation to employees and this letter does not give rise to any other relationship between you and the organisation, in particular that of an employee.

While undertaking research through the organisation you will remain accountable to your substantive employer but you are required to follow the reasonable instructions of the organisation and the nominated Manager for this work who is [PI / POC NAME] in this NHS or those instructions given on their behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by the organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with the organisations policies and procedures, which are available to you upon request, and the Research Governance Framework.

You are required to co-operate with the organisation in discharging its/their duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on the organisations premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at all times.

If you have a physical or mental health condition or disability which may affect your research role and which might require special adjustments to your role, if you have not already done so, you must notify your employer and each organisation prior to commencing your research role at that organisation.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the organisations premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that the organisation(s) do not accept responsibility for damage to or loss of personal property.

This organisation may revoke this letter and any organisation may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of the organisation or if you are convicted of any criminal offence. You

Appendix 9: Research proposal for medical record review

Research proposal for medical record review | Chrissy Bishop | Born in Bradford PhD student

Date: 21/09/2015

Overarching study aim: Investigate service provision, referral pathways and disease burden for children with complex healthcare needs.

Hypothesis: Complex healthcare needs in children are responded to with disjointed services which are associated with increased pressure on children, families and increased service utilization.

Study objectives:

Explore pathways of complexity through services for children with complex healthcare needs.
Describe and analyse trends in disease burden for children with complex healthcare needs using Born in Bradford primary care data and medical record review.
Describe and analyse frequency of service use of children with complex healthcare needs using Born in Bradford primary care data and medical record review.

Rationale and background information

Children today have a heterogeneous mix of rare diseases, without having a select few that dominate impact as in adults. Children with complex conditions encounter multiple physical, functional and psychological needs. Accurate population level estimates of child complexity requires multiple data sources in order to follow their pathways accurately and representationally. Current progress with primary care data is outlined below, supporting the request for paediatric medical records.

Primary care data

Primary care data records some information well and others not so well. Diagnoses rates, GP consultation rates and prescription rates had the least missing data thus descriptive

analyses were performed. Children with a diagnosed major congenital anomaly as classified by the International Classification of Functioning version 10 (WHO 2015), are classed as a child with complex healthcare needs in this study. We already have evidence to show children with major congenital anomalies are associated with increased healthcare needs (REF). Furthermore, prevalence rates of congenital anomalies in Bradford are confirmed as being higher than the national average, as described in the Bradford Congenital Anomalies Study (BradCAS; Sheridan et al. 2013), which found 451 children with congenital anomalies in Bradford, all part of the Born in Bradford study. With the availability of primary care data, rates of GP consultations and prescriptions were analysed for these 451 cases, in comparison to the rest of the Born in Bradford cohort whom did not have a congenital anomaly (n=12593). 4 were later dropped from the BradCAS sample, as they were not matched to GP records leaving 447. Regression analyses adjusting for ethnicity, birth weight, and a measure of material deprivation were performed

Main findings

On average children had 3-4 different congenital diagnoses simultaneously.
From BradCAS sample (n=477), the most frequently diagnosed congenital anomalies were related to the Circulatory system (14%), musculoskeletal system (14%) followed by an 'other' category (8.6%). This includes malformations not otherwise classified.
Drugs (by BNF chapter) were most frequently prescribed for nutrition and blood (30%), skin (10%) and the gastrointestinal system (9%).
Children with a low birth weight and a congenital anomaly had lower GP consultation rates than children with normal birth weight. This is an important finding and may be reflective of referrals at birth to specialists and CDC, meaning GP activity will be low.
South Asian children with congenital anomalies had higher GP consultation rates than white British children.

Interpretation given local practices

According to local practice, children with congenital anomalies and complex healthcare needs at birth are more likely to be referred to specialists such as the Child Development Centre (CDC), or to a specialist consultant dependent on diagnoses and birth complications. These children remain on CDC caseload until they reach adulthood (19y). During their time registered with CDC, these children rarely see their GP, instead using services from their hospital consultant, CDC, and community nursing teams. Information relating to referrals to specialists, assessment or diagnoses letters, a significant aspect of demonstrating

complexities of healthcare pathways are not available from primary care records. Consequently, GP primary care data does not document these children's activity well. This reduces the reliability of GP data to reflect the pathways of children with complex healthcare needs, possibly explaining the unexpected finding's from current data analysis of children with a low birth weight apparently using the GP less. This is also likely to skew prevalence rates of certain chronic conditions and congenital anomalies using primary care data alone. Primary Care data documents when a referral is made, and whether it was routine or urgent. It does not specify the recipient of the referral, or provide access to the letter sent with the referral.

Study Design

Sample selection
200 child identifiers selected with confirmed congenital anomalies.
A control group of 200 child identifiers randomly selected from the cohort without congenital anomalies.
Paediatric medical files requested for 400 children.

Methodology

Medical record data abstraction – Pre-recorded, patient-focused data.
Medical records are often noted to be the most complete and reliable data available for understanding patient care process.
Convenience sample – Dealing with rare cases thus a smaller sample size appropriate.
Coding of data extraction – Two trained coders to perform data extraction from records. One blind one not blind.
Extraction form (included) to ensure a measure of consistency among abstractors. Inter-rater reliability will be calculated using Cohen's kappa.

Data extraction

Design of the data extraction form will be finalized once records are retrieved and reviewed, to ensure forms mimic layout of the records and ask for appropriate information as available.

Envisaged sources of data.
Specialist clinic assessment letters
Discharge letters from Therapy assessments (Occupational Therapy, Physiotherapy)

Summary of treatment letters intended for the GP.
Admission notes
Discharge summaries

Limitations/methods to improve reliability

This kind of data not originally collected for research purposes. May be lacking quality and quantity.
Free text information will produce difficulties with legibility and interpretation6.
Missing data or subjects with missing data may differ systematically from other subjects. Dropping variables that are missing in at least 10% of sample may be advisable.
Inter-rater agreement will help determine how much variation between data collected is due to certain variables in the extraction form. This is a good way of dropping variables, which have a high level of disagreement5.
Abstraction forms will be piloted (yet to determine exact variables for extraction)
Variable manual to be created, including locations of variables, glossary of terms, how to deal with missing data or ambiguous meanings.

Appendix 10: Medical record abstraction form.

Medical record review extraction form

Data item	Data entry field
Patient identification	
A. Admission History	
1. Is there evidence of recent hospital admission?	1=Yes 2=No 3=Not available
2. Is there evidence of more than one hospital admission?	1=Yes 2=No 3=Not available
3. If answered yes to question 1 or 2 Was each admission planned or unplanned? Please list in date order and specify admission type.	1=Planned 2=Unplanned 3=Not available e.g Admission 1: Planned Admission 1: Admission 6: Admission 2: Admission 7: Admission 3: Admission 8: Admission 4: Admission 9 Admission 5: Admission 10:
4.Did admission note contain evidence of a serious medical event (see manual for classification of serious medical event) Please list in relation to relevant admission from question 3.	1= Yes 2= No 3= Not available e.g Admission 1: Yes Admission 1: Admission 6: Admission 2: Admission 7: Admission 3: Admission 8: Admission 4: Admission 9 Admission 5: Admission 10:
B. Referrals	
1. Is there evidence of a referral relevant to the research question? (see manual)	1=Yes 2=No 3=Not available

2. What is the type of referral	1=Child Development Centre 2=Therapy services 3=SALT 4=Surgery 5=Social Services 6= Specialist paediatric consultant 7=Other specialist yet to be defined
3. Is there evidence of more than one referral to different services?	1= Yes 2= No 3= Not available
4. Is there evidence of more than one referral to the same service but at different time periods?	1= Yes 2= No 3= Not available
5. Did any of the referrals take place at birth or within the first month of life?	1= Yes 2 = No 3 = Not available
C. Assessment letters	
If answered yes to question 1 section B 1. Is there evidence of an assessment letter associated with any/all of the referrals?	1= Yes 2= No 3= Not available
If answered Yes to question 1 section C 2. Which of the following categories does the assessment letter refer to? Circle one or more dependent on number of assessment letters found.	1=Child Development Centre 2=Therapy services 3=SALT 4=Surgery 5=Social Services 6= Specialist paediatric consultant 7=Other specialist yet to be defined
Separate questionnaire for each category of referral to be added, and data extraction questions to be added. This is likely to be subjective information and a bit tricky to operationalize. Need to see medical files before predicting this.	
E. Discharge summaries	
1. Is there evidence of a discharge summary letter associated with any/all of the referrals?	1 = Yes 2 = No 3 = Not available
2. Did the child stay in hospital for a prolonged period of time? (see manual for	1 = Yes 2 = No

prolonged defined)	3 = Not available
If answered yes to question 1 section E 3. Is there evidence of a follow-up service required from any or all of the discharge letters?	1 = Yes 2 = No 3 = Not available
4. Is there evidence of a readmission or adverse event associated with the same reason for discharge?	1 = Yes 2 = No 3 = Not available
5. Is there evidence of the child being discharged with technology dependence?	1 = Yes 2 = No 3 = Not available

Appendix 11: ICD-10 Codes included in Sheridan et al. (2013) that were not part of the EUROCAT (2013) list of congenital anomalies that require registration

D codes	E codes	G codes	H codes	K codes	P codes	R codes	U codes	I codes	N codes	L codes	J codes	F codes
D1810	E031	G111	H269	K006	P051	R18X	U720	I429	N178	L059	J380	F842
D227	E031	G119	H500	K006	P051	R628	U724	I456	N271	L219	J380	
D561	E031	G239	H500	K070	P051	R628	UM04	I471		L859	J90X	
D561	E038	G253	H500	K070	P051	R628	UM192	I471				
D561	E038	G318	H501	K219	P051	R629	UM21	I471				
D561	E038	G318	H509	K409	P051	R629	UM23	I458				
D561	E039	G318	H520	K40X	P071	R629	UM42					
D578	E039	G318	H521	K429	P072	R629	UM47					
D66X	E039	G318	H547	K550	P288	R629	UM631					
D66X	E161	G404	H547	K550	P351	R629	UM75					
D682	E162	G404	H547	K592	P599	R629	UM75					
D691	E213	G409	H55X	K831	P611	R629	UM85					
D696	E230	G409	H55X		P77X	R629	UM88					
D821	E250	G409	H903		P835	R629	UM89					

	E271	G409	H903	P835	R629
	E271	G710	H903	P835	R629
	E271	G712	H903	P90X	R629
	E291	G712	H903	P941	R629
	E291	G712	H903	P942	R629
	E343	G713	H903	P942	R629
	E343	G934	H904	P942	R629
	E538		H904	P942	R629
	E559		H905		R629
	E700		H905		
	E703		H905		
	E703		H905		
	E711		H905		
	E711		H905		
	E711		H905		
	E711		H905		
	E721		H919		
	E722		H919		
	E722		H919		
	E740		H919		
	E742		H919		

E742	H919
E752	H919
E752	H919
E752	H919
E752	
E752	
E752	
E770	
E770	
E770	
E770	
E798	
E805	
E805	
E832	
E841	
E849	
E849	
E872	
E872	
E888	

E888	
E888	
E889	
E889	

Appendix 12: Search strategy healthcare use

MeSH search

1	Exp Congenital Abnormalities	316853
2	Genetic diseases.mp	15857
3	Exp Genetic research/economics	243
4	Exp genetic determinism	261
5	Direct Service Costs/sn, td [Statistics & Numerical Data, Trends]	139
6	Health Services Accessibility/ec, og, sn, td [Economics, Organization & Administration, Statistics & Numerical Data, Trends]	11798
7	Health Services Accessibility/ or *Primary Healthcare/ or *"Delivery of Healthcare"	99692
8	Direct Service Costs/sn, td [Statistics & Numerical Data, Trends]	139
9	Hospitalization/ec, sn, td, ut [Economics, Statistics & Numerical Data, Trends, Utilization]	13952
10	Length of Stay"/ec, sn, td [Economics, Statistics & Numerical Data, Trends]	4658
11	General Practice/ec, og, sn, td [Economics, Organization & Administration, Statistics & Numerical Data, Trends]	1369

12	Primary Healthcare/ec, sn, td, ut [Economics, Statistics & Numerical Data, Trends, Utilization]	6397
13	Cost of Illness"/ or *Healthcare Costs/	23719
14	Health Services Research/ or *"Health Services Needs and Demand"/	24389
15 to GP use and CA	11 OR 12	7706
16	1 OR 2 OR 3 OR 4	331147
17	5 OR 6 Or 7 OR 8 OR 9 OR 10 OR 13 OR 14	159518
18	15 AND 16 AND 17	6
19 – Hospitalization and secondary care and CA	9 OR 10	18280
20	5 OR 6 OR 7 OR 8 OR 13 OR 14	142706
21	19 AND 20 AND 16	15
22 – All terms related to healthcare use, all terms for CA.	5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14	
23	22 AND 16	826
24	limit 20 to (English language and humans and yr="2012 to Current")	351

Key words search

1	"congenital malformation$".ti,ab,kf.	7800
2	"congenital anomal$".ti,ab,kf.	11176

3	"congenital abnormalit$".ti,ab,kf.	3905
4	"congenital defect$".ti,ab,kf.	2445
6	"birth injur$".ti,ab,kf.	526
7	"congenital deformit$".ti,ab,kf.	537
9	"genetic diseas$".ti,ab,kf.	9400
10	general practice.ti,ab,kf.	19732
11	GP.ti,ab,kf.	28106
12	Primary Care.ti,ab,kf.	79134
13	utili#ation.ti,ab,kf.	108487
14	indirect cost$.ti,ab,kf.	3877
15	access to care.ti,ab,kf.	7358
16	cost of illness.ti,ab,kf.	1199
17	burden.ti,ab,kf.	116876
18	"service us$".ti,ab,kf.	8660
19	"hidden cost$".ti,ab,kf.	269
20	"coordination".ti,ab,kf.	54371
21	"hospitali#ation".ti,ab,kf.	81200
22	"hospital admission$".ti,ab,kf.	24018
23	"length of stay".ti,ab,kf.	33062
24 – GP	10 OR 11 OR 12	117284
25	13 OR 14 OR 15 OR 16 OR	291092

	17 OR 18 OR 19 OR 20	
26 – Hospital	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9	34386
27	24 AND 25 AND 26	6
28	21 OR 22 OR 23	128419
26	24 AND 25 AND 26	28
27 – All GP and Hospital, Healthcare resource AND CA	10 OR 11 OR 12 OR 21 OR 22 OR 23	215224
28	27 AND 25 AND 26	20

Appendix 13: Search strategy for Undiagnosed diseases

MeSH terms search

Note: There are no MeSH terms for undiagnosed

1	Exp Congenital Abnormalities	316853
2	Genetic diseases.mp	15857
3	Exp Genetic research/economics	243
4	Exp genetic determinism	261
5	Direct Service Costs/sn, td [Statistics & Numerical Data, Trends]	139
6	Health Services Accessibility/ec, og, sn, td [Economics, Organization & Administration, Statistics & Numerical Data, Trends]	11798
7	Health Services Accessibility/ or *Primary Healthcare/ or *"Delivery of Healthcare"	99692
8	Direct Service Costs/sn, td [Statistics & Numerical Data, Trends]	139
9	Hospitalization/ec, sn, td, ut [Economics, Statistics & Numerical Data, Trends, Utilization]	13952
10	Length of Stay"/ec, sn, td [Economics, Statistics & Numerical Data, Trends]	4658
11	General Practice/ec, og, sn, td [Economics, Organization	1369

	& Administration, Statistics & Numerical Data, Trends]	
12	Primary Healthcare/ec, sn, td, ut [Economics, Statistics & Numerical Data, Trends, Utilization]	6397
13	Cost of Illness"/ or *Healthcare Costs/	23719
14	Health Services Research/ or *"Health Services Needs and Demand"/	24389

Step 2

Key terms search – Medline and Ovid database

SearchNo.	Search term	Database AMED, HMIC, MIDIRS, PsycINFO, OpenGrey, Reviews	Ovid, MEDLINE
15	"congenital malformation$".ti,ab,kf.	1806	7800
16	"congenital anomal$".ti,ab,kf.	2075	11176
17	"congenital abnormalit$".ti,ab,kf.	896	3905
18	"congenital defect$".ti,ab,kf.	247	2445
19	"birth injur$".ti,ab,kf.	203	526
20	"congenital deformit$".ti,ab,kf.	35	537

21	"genetic diseas$".mp	676	9400
22	“genetic condition$”.mp	565	1791
23	“rare syndrome$”.mp	129	1378
24	“intellectual disability$”.mp	14037	20909
25	“Learning disability$”.mp	20612	4373
26	“Unknown mutation$”.mp	21	492
27	“atypical presentation$”.mp	331	3131
28	“undiagnosed”.mp	2079	11715
29	“undiagnosed genetic condition$”.mp	0	7
30	“unknown disease$”.mp	27	258
31	“unknown condition$”.mp	22	72
32	"non-specific symptom$”.mp	114	1122
33	“Syndrome$ without a name”.mp”	0	
33	“GP”.ti,ab,kf.	11359	28106
34	“general practice”.ti,ab,kf.	11344	19732
35	“Primary Care”.ti,ab,kf.	40801	79134
36	“utili#ation”.ti,ab,kf.	26150	108487
37	“indirect cost$”.ti,ab,kf.	958	3877
38	“access to care”.ti,ab,kf.	3246	7358
39	“cost of illness”.ti,ab,kf.	313	1199

40	“burden”.ti,ab,kf.	29188	116876
41	"service us$".ti,ab,kf.	12740	8660
42	"hidden cost$".ti,ab,kf.	218	269
43	"coordination".ti,ab,kf.	17237	54371
44	"hospitali#ation".ti,ab,kf.	15293	81200
45	"hospital admission$".ti,ab,kf.	5618	24018
46	"length of stay".ti,ab,kf.	5996	33062
47	“born”.mp	37153	74558
48	“birth”.mp	99449	198609
49	“birth rate”.mp	2608	6620
50	“prevelance”.mp	68	94
51	“incidence”.mp	49945	522385
52	“Test$”.mp	553083	2408830
53	“genome sequencing”.mp	415	27605
54	“sequencing”.mp	6466	147054
55	“whole genome sequencing”.mp	204	3945
56	“NGS”.mp	123	3235
57	“Next generation sequencing”.mp	406	11206
58	“exome sequencing”.mp	681	4773
59	“Global developmental delay”.mp	4	16
60	“Failure to thrive”.mp	495	3889
61	“dysmorphic features”.mp	225	2106

62	“hypertonia”.mp	319	1428
63	“hypotonia”.mp	729	5534
64	“hypermobility”.mp	305	1799
65	“hypomobility”.mp	54	203
66	“feeding difficult$”.mp	492	1253
67	“tube feed$”.mp	484	2347
68	“unsafe swallow”.mp	0	7
69 – MeSH terms AND key terms related to healthcare use	5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 [MeSH] OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 [Key terms]	Key terms only = 970470	3790964
70– MeSH terms AND key terms related to CA and genetic conditions	1 OR 2 OR 3 OR 4 [MeSH] OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 [Key terms]	11089	348010
71 – Key terms for undiagnosed	26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 [Key terms]	2590	15636
72 – Combine	69 AND 70 AND 71	78	523
73	Limit 73 to (English language and humans)	75	467
SUB SEARCH			
74	59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68	2914	17456
75	71 AND 74	17	105

Appendix 14: Supporting parents and carers PRISMA and Search strategyMedline search

1	Exp mother/	27919
2	Exp parent/	76472
3	Exp father/	6501
4	(Mother$ or mom$ or Mum$).ti	52066
5	(Parent$ or Maternit$ OR Maternal OR Paternal OR parenthood$ OR motherhood OR fatherhood OR blood relation$).ti	128488
6	(Carer$ OR guardian$ OR Formal carer$ OR Informal carer$ OR caregiver$).ti (MeSH)	13078
7	(Basic psychological need$ OR psychological stressor$ OR psychological theor$ OR psychological side effect$ OR psychological resilience OR psychological side effect$ OR psychological stress$).ti	1846
8	(Competenc$ OR capability$ OR proficienc$ or Relatedness or autonomy$ OR self-sufficiency OR independen$ OR free will (MeSH) OR paternalism OR Self determination theory).ti (MeSH)	956157
9	(Carer burnout OR carer breakdown OR carer exhaustion).ti	0
10	(Self esteem (MeSH) OR self concept (MeSH) or Need satisfaction).ti.	18235
11	(Mother-child relation$ OR mother-child interaction$ OR mother-infant relation$ OR mother-infant interaction$).ti	749
12	(Parental confidence OR Mothers wellbeing OR Maternal behaviour OR maternal care pattern$ (MeSH) OR Paternal behaviour OR paternal	417

	care pattern$ (MeSH) OR Parenting style$).ti	
13	(Family wellbeing OR family health OR family welfare OR Happiness OR contentment OR Life satisfaction OR life fulfilment OR Self actualization).ti	3637
14	1 OR 2 OR 3 OR 4 OR 5 OR 6	227672
15	7 OR 8 OR 10	96156
16	11 OR 12 OR 13	4800
17	14 AND 15 AND 16	18

PsycINFO search

1	mother	73769
2	Parent	113184
3	Father	32879
4	(Mother$ or mom$ or Mum$).ti	30181
5	(Parent$ or Maternit$ OR Maternal OR Paternal OR parenthood$ OR motherhood OR fatherhood OR blood relation$).ti	84221
6	(Carer$ OR guardian$ OR Formal carer$ OR Informal carer$ OR caregiver$).ti (MeSH)	11413
7	(Basic psychological need$ OR psychological stressor$ OR psychological theor$ OR psychological side effect$ OR psychological resilience OR psychological side effect$ OR psychological stress$).ti	2187
8	(Competenc$ OR capability$ OR proficienc$ or Relatedness or autonomy$ OR self-sufficiency OR independen$ OR free will (MeSH) OR paternalism OR Self determination theory).ti (MeSH)	35548
9	(Carer burnout OR carer breakdown OR carer exhaustion).ti	0
10	(Self esteem (MeSH) OR self concept (MeSH) or Need satisfaction).ti.	19133
11	(Mother-child relation$ OR mother-child interaction$ OR mother-infant relation$ OR mother-infant interaction$).ti	1636
12	(Parental confidence OR Mothers wellbeing OR Maternal behaviour OR maternal care pattern$ (MeSH) OR Paternal behaviour OR paternal	1174

	care pattern$ (MeSH) OR Parenting style$).ti	
13	(Family wellbeing OR family health OR family welfare OR Happiness OR contentment OR Life satisfaction OR life fulfilment OR Self actualization).ti	7170
14	1 OR 2 OR 3 OR 4 OR 5 OR 6	231854
15	7 OR 8 OR 10	56491
16	11 OR 12 OR 13	9968
17	14 AND 15 AND 16	147
18	Limit to English language and yr 2000 to Current	63
19	(healthcare use$ OR healthcare utili#ation OR healthcare access OR GP visit$).ti	869
20	14 AND 19	67